REGULATORY REFORM SERIES, PART 5—FDA MEDICAL DEVICE REGULATION: IMPACT ON AMERICAN PATIENTS, INNOVATION, AND JOBS

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

ONE HUNDRED TWELFTH CONGRESS

FIRST SESSION

JULY 20, 2011

Serial No. 112–78

Printed for the use of the Committee on Energy and Commerce
energycommerce.house.gov

U.S. GOVERNMENT PRINTING OFFICE

73–314 PDF WASHINGTON : 2012

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

COMMITTEE ON ENERGY AND COMMERCE

FRED UPTON, Michigan
Chairman

JOE BARTON, Texas
Chairman Emeritus
CLIFF STEARNS, Florida
ED WHITFIELD, Kentucky
JOHN SHIMKUS, Illinois
JOSEPH R. PITTS, Pennsylvania
MARY BONO MACK, California
GREG WALDEN, Oregon
LEE TERRY, Nebraska
MIKE ROGERS, Michigan
SUE WILKINS MYRICK, North Carolina
Vice Chairman
JOHN SULLIVAN, Oklahoma
TIM MURPHY, Pennsylvania
MICHAEL C. BURGESS, Texas
MARSHA BLACKBURN, Tennessee
BRIAN P. BILBRAY, California
CHARLES F. BASS, New Hampshire
PHIL GINGREY, Georgia
STEVE SCALISE, Louisiana
ROBERT E. LATTA, Ohio
CATHY McMORRIS RODGERS, Washington
GREGG HARPER, Mississippi
LEONARD LANCE, New Jersey
BILL CASSIDY, Louisiana
BRETT GUTHRIE, Kentucky
PETE OLSON, Texas
DAVID B. McKINLEY, West Virginia
CORY GARDNER, Colorado
MIKE POMPEO, Kansas
ADAM KINZINGER, Illinois
H. MORGAN GRIFFITH, Virginia

HENRY A. WAXMAN, California
Ranking Member
JOHN D. DINGELL, Michigan
Chairman Emeritus
EDWARD J. MARKEY, Massachusetts
EDOLPHUS TOWNS, New York
FRANK PALLONE, JR., New Jersey
BOBBY L. RUSH, Illinois
ANNA G. ESHOO, California
ELIOT L. ENGEL, New York
GENE GREEN, Texas
DIANA DEGETTE, Colorado
LOIS CAPPS, California
MICHAEL F. DOYLE, Pennsylvania
JANICE D. SCHAKOWSKY, Illinois
CHARLES A. GONZALEZ, Texas
JAY INSLEE, Washington
TAMMY BALDWIN, Wisconsin
MIKE ROSS, Arkansas
ANTHONY D. WEINER, New York
JIM MATHESON, Utah
G.K. BUTTERFIELD, North Carolina
JOHN BARROW, Georgia
DORIS O. MATSUI, California
DONNA M. CHRISTENSEN, Virgin Islands
KATHY CASTOR, Florida

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

CLIFF STEARNS, Florida
Chairman

LEE TERRY, Nebraska
SUE WILKINS MYRICK, North Carolina
JOHN SULLIVAN, Oklahoma
TIM MURPHY, Pennsylvania
MICHAEL C. BURGESS, Texas
MARSHA BLACKBURN, Tennessee
BRIAN P. BILBRAY, California
PHIL GINGREY, Georgia
STEVE SCALISE, Louisiana
CORY GARDNER, Colorado
H. MORGAN GRIFFITH, Virginia
JOE BARTON, Texas
FRED UPTON, Michigan *(ex officio)*

DIANA DEGETTE, Colorado
Ranking Member
JANICE D. SCHAKOWSKY, Illinois
MIKE ROSS, Arkansas
KATHY CASTOR, Florida
EDWARD J. MARKEY, Massachusetts
GENE GREEN, Texas
DONNA M. CHRISTENSEN, Virgin Islands
JOHN D. DINGELL, Michigan
HENRY A. WAXMAN, California *(ex officio)*

C O N T E N T S

REGULATORY REFORM SERIES, PART 5—FDA MEDICAL DEVICE REGULATION: IMPACT ON AMERICAN PATIENTS, INNOVATION, AND JOBS

WEDNESDAY, JULY 20, 2011

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATION,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:02 a.m., in room 2322 of the Rayburn House Office Building, Hon. Cliff Stearns (chairman of the subcommittee) presiding.

Members present: Representatives Stearns, Terry, Myrick, Sullivan, Burgess, Blackburn, Bilbray, Gingrey, Scalise, Gardner, Griffith, Lance, Barton, DeGette, Schakowsky, Green, Christensen, Dingell and Waxman (ex officio).

Staff present: Clay Alspach, Counsel, Health; Carl Anderson, Counsel, Oversight; Karen Christian, Counsel, Oversight; Todd Harrison, Chief Counsel, Oversight and Investigations; Sean Hayes, Counsel, Oversight and Investigations; Sean Hayes, Counsel, Oversight and Investigations; Kirby Howard, Legislative Clerk; Debbee Keller, Press Secretary; Ryan Long, Chief Counsel, Health; Carly McWilliams, Legislative Clerk; Alan Slobodin, Deputy Chief Counsel, Oversight; Sam Spector, Counsel, Oversight; John Stone, Associate Counsel; Tim Torres, Deputy IT Director; Kristin Amerling, Democratic Chief Counsel and Oversight Staff Director; Phil Barnett, Democratic Staff Director; Stacia Cardille, Democratic Counsel; Stephen Cha, Democratic Senior Professional Staff Member; Brian Cohen, Democratic Investigations Staff Director and Senior Policy Advisor; Eric Flamm, FDA Detailee; Karen Lightfoot, Democratic Communications Director and Senior Policy Advisor; Ali Neubauer, Democratic Investigator; and Mitch Smiley, Democratic Assistant Clerk.

Mr. STEARNS. Good morning, everybody, and the subcommittee will come to order and I will open with my opening statement.

OPENING STATEMENT OF HON. CLIFF STEARNS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

We convene this hearing of the Subcommittee on Oversight and Investigations to examine FDA's medical device regulations and their impact on American patients, innovation and jobs. The medical device industry has brought hundreds of thousands of high-

paying jobs to our country and life-saving, life-improving devices to our Nation's patients in a safe and efficient manner.

Unfortunately, it appears that regulatory inconsistency and inefficiency at FDA is causing innovative medical device companies to move offshore and launch their products abroad, oftentimes years before they enter the U.S. market, if at all. These are systemic problems at the Center for Devices and Radiological Health, CDRH, that must be resolved that are not a matter of funding.

A Congressional Research Service report issued in April 2010 found that medical device review process funding increased from $275 million in fiscal year 2008 to $368 million in fiscal year 2010. This represents nearly a 35 percent increase in funding. Comparing 2010 with the 2003 to 2007 time period, the average review time for lower-risk devices approved through the 510(k) process increased by 43 percent and the average review time for higher-risk, innovative devices under the premarket approval system increased 75 percent.

President Obama himself has acknowledged that he has gotten a lot of commentary about the fact that essentially FDA's model was designed for the kind of medical devices you see in museums. In reference to his Administration's purported commitment to regulatory reform, he noted that this would be an area where they should be "getting a group to think strategically about how we design these regulatory bodies so that they are up to speed and more responsive in a dynamic economy." Unfortunately, in the eyes of the Administration, this group does not appear to include the innovative, job-creating companies or the very patients that these devices are designed to help.

For example, FDA commissioned the Institute of Medicine, IOM, to review the current 510(k) process and consider a number of specific issues related to the improvement of device regulations. Not a single company or industry representative that is impacted by these regulations is on the panel. Judging from a letter sent by Senator Al Franken to CDRH Director, Jeffrey Shuren, our witness today, Senator Franken and others share my concerns. In it, he states, "I believe that the medical device industry contains a wealth of expertise that is too often neglected when considering changes to the device review process. I strongly encourage you to establish a clear process for soliciting and considering the suggestions and concerns of the medical device industry on any and all recommendations made by the IOM before finalizing or implementing any changes to the process." In addition to the stunning lack of industry representation, there is not a single patient representative on the panel. This is not acceptable and does not comply with President Obama's call for allowing "public participation and an open exchange of ideas."

In addition, CDRH is supposed to "use the least burdensome" tools for achieving regulatory ends. This is not only a key tenet of the President's Executive Order on Regulatory Reform, but required by the Food and Drug Modernization Act of 1997. Specifically, in order to improve regulatory efficiency of the 510(k) and premarket approval process, Congress mandated that the FDA eliminate unnecessary burdens that may delay the marketing of beneficial new products and only request the least burdensome in-

formation necessary to make those determinations. Unfortunately, FDA appears to be actively thwarting the mandates of Congress and fostering regulatory uncertainty by reducing its use of the least burdensome provisions.

Now, whether this is a calculated effort or a lack of leadership in promoting such principles, the end result is equally unacceptable: companies closing their doors and moving abroad; patients in the United States waiting for innovative treatments or being forced themselves to go abroad to get them.

We will hear today from several of these patients. Hopefully, Dr. Shuren will gain some insight from these experiences and better understand the fact that patient safety and public health are not only jeopardized by approving devices that are unsafe, but also by failing to approve devices that are safe. Such poor processes and decision-making also stifle innovation, cutting-edge American companies that create numerous badly needed jobs here in the United States. As FDA Commissioner Hamburg said just this past week, "This is a critical time for innovation." She acknowledged that FDA has played a role in the national decline in medical product innovation, adding that she felt much of the criticism of her agency was deserved. Hopefully we can find some solutions to reverse this alarming trend today and soon. Patients are waiting.

[The prepared statement of Mr. Stearns follows:]

Opening Statement of the Honorable Cliff Stearns
Chairman, Subcommittee on Oversight and Investigations
"Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs"
July 20, 2011
(Remarks as Prepared for Delivery)

We convene this hearing of the Subcommittee on Oversight and Investigations to examine FDA's medical device regulations and their impact on American patients, innovation, and jobs. The medical device industry has brought hundreds of thousands of high-paying jobs to our country and life-saving, life-improving devices to our nation's patients in a safe and efficient manner. Unfortunately, it appears that regulatory inconsistency and inefficiency at FDA is causing innovative medical device companies to move offshore and launch their products abroad, oftentimes years before they enter the U.S. market, if at all. These are systemic problems at the Center for Devices and Radiological Health (CDRH) that must be resolved that are not a matter of funding. A Congressional Research Service report issued in April 2010 found that medical device review process funding increased from $275 million in FY2008 to $368 million in FY2010. This represents a nearly 35% increase in funding. Comparing 2010 with the 2003 to 2007 time period, the average review time for lower-risk devices approved through the 510(k) process increased by 43% and the average review time for higher-risk, innovative devices under the Premarket Approval system increased 75%.

President Obama himself has acknowledged that he has "gotten a lot of commentary about the fact that ... essentially [FDA's] model was designed for the kind of medical devices you see in museums." In reference to his Administration's purported commitment to regulatory reform, he noted that this would be an area where they should be "getting a group to think strategically about how we design these regulatory bodies so that they are up to speed and more responsive to a dynamic economy." Unfortunately, in the eyes of the Administration, this group does not appear to include the innovative, job-creating companies or the very patients that these devices are designed to help.

For example, FDA commissioned the Institute of Medicine (IOM) to review the current 510(k) process and consider a number of specific issues related to the improvement of device regulations. Not a single company or industry representative that is impacted by these regulations is on the panel. Judging from a letter sent by Senator Al Franken to CDRH Director, Jeffrey Shuren (our witness today), Senator Franken and others share my concerns. In it he states, "I believe that the medical device industry contains a wealth of expertise that is too often neglected when considering changes to the device review process. I strongly encourage you to establish a clear process for soliciting and considering the suggestions and concerns of the medical device industry on any and all recommendations made by the IOM before finalizing or implementing any changes to the process." In addition to the stunning lack of industry representation, there is not a single patient representative on the panel. This is not acceptable and does not comply with President Obama's call for allowing "public participation and an open exchange of ideas."

In addition, CDRH is supposed to "use the 'least burdensome' tools for achieving regulatory ends." This is not only a key tenet of the President's Executive Order on Regulatory Reform, but required by the Food and Drug Modernization Act of 1997. Specifically, in order to improve regulatory efficiency of the 510(k) and premarket approval process, Congress mandated that FDA eliminate unnecessary burdens that may delay the marketing of beneficial new products and only request the least burdensome information necessary to make those determinations. Unfortunately, FDA appears to be actively thwarting the mandates of Congress and fostering regulatory uncertainty by reducing its use of the "least burdensome" provisions. Whether this is a calculated effort or a lack of leadership in promoting such principles, the end result is equally unacceptable—companies closing their doors and moving abroad; patients in the U.S waiting for innovative treatments or being forced to go abroad to get them.

We will hear today from several of these patients. Hopefully Dr. Shuren will gain some insight from their experiences and better understand the fact that patient safety and public health are not only jeopardized by approving devices that are unsafe, but also by failing to approve devices that are safe. Such poor processes and decision-making also stifle innovation, cutting-edge American companies that create numerous badly-need jobs here in the U.S. As FDA Commissioner Hamburg said just this past week, "This is a critical time for innovation." She acknowledged that FDA has played a role in the national decline in medical product innovation, adding that she felt much of the criticism of her agency was "deserved." Hopefully we can find some solutions to reverse this alarming trend soon. Patients are waiting.

Mr. STEARNS. With that, I recognize the ranking member, Ms. DeGette.

OPENING STATEMENT OF HON. DIANA DEGETTE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF COLORADO

Ms. DEGETTE. Thank you very much, Mr. Chairman, for holding this hearing.

The topic of medical devices hits very close to home with me and I am very, very interested in this topic, because just like Ms. Sagan's daughter, my daughter, Francesca, has type 1 diabetes and has had type 1 diabetes for 13 years, and so I know every day what children living with these diseases, and young adults living with these diseases need to do with devices—blood sugar monitoring, making sure they eat healthy meals and daily exercise. For the generation of kids like our two kids, Ms. Sagan's and mine, the short-term cure is medical devices. My daughter and probably Ms. Sagan's daughter uses an insulin pump and a continuous glucose monitor every day and yet—Ms. Sagan, I read your testimony and it broke my heart because every single parent who has a child living with this disease knows the scary low blood sugars and the scary thought about some of the consequences that can happen with this disease, but for our children, good devices have been the cures and the treatment for them and what will continue to be the treatments for them in their lives.

Now, unfortunately, some of the advances in these technologies, not just for diabetics but for other diseases, seem to so many of us to have been so slow over at the FDA, and the perfect example is in Ms. Sagan's testimony where she talks about our efforts to get a continuous glucose monitor approved that would send a message to the pump and would cut off insulin flow if the blood sugar is way too low.

Mr. Chairman, I want to thank you and many members of this committee for signing a letter by the Diabetes Caucus urging the FDA to look at this device because it can literally save lives, and we appreciate it, and this is true not just for these devices but for devices that millions of Americans use for countless different diseases. On the one hand, people are relying on devices, and on the other hand, we want to make sure that improvements and advances in those devices and new devices are approved with speed. But on the other hand, we need to make sure that the FDA has the appropriate tools to make sure that medical device approval process helps encourage innovation while at the same time protecting patient safety, and that's the challenge I think that the FDA faces and I think that that's the challenge that we all face on this committee is making sure that while we support the FDA expediting an approval process that we make sure that the reviews are done in a way that is safe for those patients and for those devices. We need to find the right balance and we can't pretend that there aren't sometimes tradeoffs between safety and speed.

Now, I am sympathetic to the industry concerns we hear today but I also fear that too often the device industry and also people like me who are eager to see cures and treatments for diseases kind of minimize those tradeoffs between safety and speech. Two

studies funded by the medical device industry, one conducted by Dr. Josh Makower and the other by the California Healthcare Institute, that have been heavily cited by many of our colleagues and by proponents of weakening FDA regulations provide a good example of how facts can be twisted. These studies have been heavily cited, and so our committee staff asked a panel of distinguished outside reviewers to analyze the methodology of these studies, and at the staff's request, officials from the FDA also submitted comments on the studies.

Mr. Chairman, Democratic committee staff prepared a supplemental memo summarizing the expert reviews of these industry studies, and I would ask unanimous consent to include this memo and the letters from FDA and the independent experts in today's hearing record.

Mr. STEARNS. I thank the gentlelady. Can we just have a copy of it and we will read it and we will look at it.

Ms. DEGETTE. You bet.

The reviewers found the following problems with these industry-funded studies. First, the existence of "so many flaws in design and execution that the authors' conclusions are rendered essentially meaningless." Second, a "woefully inadequate" response rate of only 20 percent, a biased group of respondents that included companies that had never gone through the process of getting a product reviewed by the FDA, a subjective, apples to oranges, and especially troublesome conclusion regarding the difference in approval times between the European Union and the United States, the failure to provide any evidence that a U.S. delay in approval and availability leads to adverse health outcomes. The journal editors concluded that the studies would not be fit for publication in a peer-reviewed journal.

And so as we consider the role of the FDA, we have got to rely on the facts. The patients and their families and the industry need to know how can we have the quickest review process possible while at the same time ensuring patient safety and efficacy of the devices.

So I thank you for having this hearing. I look forward to both of our panels of testimony, and I yield back.

[The prepared statement of Ms. DeGette follows:]

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED TWELFTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING

WASHINGTON, DC 20515–6115

Majority (202) 225-2927
Minority (202) 225-3641

Opening Statement of Rep. Diana DeGette
Ranking Member, Subcommittee on Oversight and Investigations
"Regulatory Reform Series #5 – FDA Medical Device Regulation: Impact on American Patients, Innovation, and Jobs"
Subcommittee on Oversight and Investigations
July 20, 2011

Thank you, Chairman Stearns. I appreciate the opportunity to participate in today's hearing to examine the role of the Food and Drug Administration in bringing medical devices to market as safely and quickly as possible.

This topic is incredibly important to me. One of my daughters has Type I diabetes. So I know first-hand how each day, children living with diabetes must balance their injections with blood sugar monitoring, healthy meals, and daily exercise. Health care costs related to diabetes total more than $174 billion each year.

We must ultimately find a cure. But right now we must support the work of medical device innovators to develop technologies like insulin pumps and CGM's that are critical in enabling young people with Type I diabetes to live a healthy life.

We need to make sure FDA has appropriate tools to ensure the medical device approval process helps these innovators and protects patient safety. So I look forward to hearing from Dr. Jeff Shuren, the Director for the Center of Devices and Radiological Health, on ways the current process can be improved.

Last month, FDA took an important step in advancing the development of an artificial pancreas system glucose suspend system, which is the predecessor to a full artificial pancreas system. I look forward to hearing more about the specific steps the agency is taking to assist in the development of these critical devices.

FDA must be able to bring these and other medical devices to market as quickly as possible while ensuring their safety to the American public.

Mr. Chairman, as we hear from our witnesses today, we need to keep in mind that the second part of that sentence – ensuring the safety of patients – is just as important as the first part – bringing devices to market as quickly as possible.

We need to find the right balance, and we cannot pretend that there aren't sometimes trade-offs between safety and speed.

While I am sympathetic to some of the industry concerns we will hear today, I do fear that all too often the device industry and its allies try to blur those trade-offs between safety and speed.

Two studies funded by the medical device industry – one conducted by Dr. Josh Makower and the other by the California Healthcare Institute – that have been heavily cited by my Republican colleagues and by proponents of weakening FDA regulations provide a good example of how facts can be twisted.

Because they have been so heavily cited, Committee staff asked a panel of distinguished outside reviewers to analyze the methodology of these studies. At the staff's request, officials from FDA also submitted comments on the studies.

Mr. Chairman, Democratic Committee staff prepared a supplemental memo summarizing the expert reviews of these industry studies. I ask unanimous consent to include this memo, and the letters from FDA and the independent experts, in today's hearing record.

The reviewers found the following problems with these industry-funded studies:

- The existence of "so many flaws in design and execution that the authors' conclusions are rendered essentially meaningless."
- A "woefully inadequate" response rate of only 20%.
- A biased group of respondents that included companies that "had never gone through the process of getting a product reviewed by the FDA."
- A "subjective," "apples to oranges," and "especially troublesome" conclusion regarding the difference in approval times between the European Union and the United States.
- The failure to provide "any evidence that [an U.S.] delay in approval and availability leads to adverse health outcomes."

The journal editors concluded that the studies would not be fit for publication in a peer-reviewed journal. As we consider the role of the FDA, we must rely on the facts. The expert analysis of these two studies shows the pitfalls of relying on one-sided analyses of problems in the device industry.

Mr. Chairman, there is one way to both speed up the approval process and make patients safer – by making sure that FDA has the resources it needs to get the job done. The Republican budget seeks to cut FDA's funding by approximately $241 million. These cuts, if enacted, will have a significant impact on the ability of FDA to do its job, including the efficient approval of medical devices. Massive cuts in FDAs budget will lead to the worst of both worlds – failure to protect patients and failure to get devices to the market quicker. We cannot let this happen.

Mr. Chairman, I thank you for holding this hearing today and I look forward to hearing from our witnesses today.

Mr. STEARNS. I thank the gentlelady, and the gentleman from Texas, Mr. Barton, is recognized for 1 minute.

OPENING STATEMENT OF HON. JOE BARTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BARTON. Thank you, Mr. Chairman. Thank you and Ranking Member DeGette for holding this oversight hearing.

The issues that we are discussing today have the ability to harm our sick, inhibit innovation and stifle domestic economic jobs and growth. On the other hand, if done properly, they have the ability to bring state-of-the-art medical devices quickly and efficiently to not only the United States citizenry but to people all over the world. I hate to say it, but the medical device review process at the Food and Drug Administration in my opinion has become overly burdensome, unpredictable and inconsistent under its current leadership.

I would like to read briefly a paragraph from the document that was prepared for this hearing, which is common themes raised by the device companies seeking FDA approval include unclear guidance, high turnover of review staff, impractical clinical designs, changing the goalpost, reluctance to approval protocols, and duplicative or overly burdensome data requests.

Hopefully, this hearing will lead to some soul searching at the FDA, and if necessary, it may lead to some legislative solutions recommended by this subcommittee to the legislative subcommittees.

I will put the rest of my statement in the record, Mr. Chairman, but this is an important hearing and it has important implications for the country.

[The prepared statement of Mr. Barton follows:]

Opening Statement of the Honorable Joe Barton
Chairman Emeritus, Committee on Energy and Commerce
Subcommittee on Oversight & Investigations Hearing
"Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation, and Jobs"
July 20, 2011

Thank you Mr. Chairman for holding this hearing. Unfortunately, the issues we are discussing today harm the sick, inhibit innovation and stifle domestic economic and job growth. The Medical Device Review Process at the Food and Drug Administration (FDA) has become overly burdensome, unpredictable and inconsistent under its current leadership. I have been committed to the advancement of the medical device industry and improving patient access since the early 1990's. In fact, I held oversight hearings on this issue back then.

American patients want and deserve access to the most advanced products on the market and are traveling to Canada and Europe to get them and seek treatment. Small companies and entrepreneurs want to create businesses and design products that will help save lives and be profitable. For this to happen, we need a regulatory system that is predictable, consistent and open. These words do not describe the current regulatory environment at the FDA, especially at the Center for Devices and Radiological Health.

I hope that Dr. Shuren, the Director of this Center, listens carefully to the first panel of witnesses who will explain how actions taken at FDA directly impact

their lives, their health, and our collective prosperity. Regulations have consequences and the benefits should outweigh the costs. This hearing exposes the problems associated with unnecessary red-tape and it is time the leadership at the FDA did something to fix it. If they are unwilling to do so, they should be replaced.

Thank you Mr. Chairman.

Mr. STEARNS. I thank the gentleman.

The gentleman from Texas, Dr. Burgess, is recognized for 1 minute.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. Thank you, Mr. Chairman, and Dr. Shuren, thank you for being here. Thank you for your willingness to hear from the panel and of course I want to thank our panelists for being here. Ms. Conger, thank you for reminding us if we are not careful, NIH stand in the future for Not Invented Here.

Now, the FDA is not interactive, it is unpredictable and discourages innovation, and this ultimately hurts patients. We don't want the FDA to approve anything that will harm people. We don't want you to simply adopt European standards. But we do want you to understand that a little predictability can go a long way. We want you held to your own standards. If you say 30 days, we shouldn't have to ask how long is that in FDA days. If a company is asked to provide proof the device does something it wasn't designed to do and they tell you that, you can't claim that as an example of noncompliance. I know you care about the FDA. You know I care about the FDA. And you do have a critically important job, but don't hide behind a twisted interpretation of benchmarks.

The truth, the doctors of tomorrow are going to have tools at their disposal that are unlike anything that you or I imagined during our training. The ability to alleviate human suffering is going to be on a scale never imagined before by any other generation of doctors. It is our job to be certain that the tools get into their hands.

Thank you, Mr. Chairman. I will yield back.

Mr. STEARNS. I recognize the gentleman from Georgia, Dr. Gingrey, for 1 minute.

OPENING STATEMENT OF HON. PHIL GINGREY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. GINGREY. Mr. Chairman, thank you.

I focused my opening statement during the July 11th prescription drug user fee hearing on my intent to pursue regulatory reform through PDUFA reauthorization building on the steps that the FDA and Dr. Hamburg have already taken. The same is true for medical devices. Patients, industry and the FDA can benefit from a more predictive regulatory framework. With limited financial resources, as outlined by the chairman, both within the FDA and in industry, it appears that an approval approach that is able to maximize effort is one that will benefit all, and I believe that if the FDA is going to be successful and becoming more responsive to new technologies and products, it is going to need the support of industry experts, patient advocates and other agencies.

I look forward to working with this committee and Dr. Hamburg to ensure we achieve this worthy goal. I thank both panels of witnesses. We look forward to hearing from you, and I yield back.

Mr. STEARNS. I thank the gentleman.

The gentleman from Nebraska, Mr. Terry, is recognized for 1 minute.

OPENING STATEMENT OF HON. LEE TERRY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEBRASKA

Mr. TERRY. Thank you. My statement is going to reference the February 9th article from the New York Times that I would like to submit for the record, unanimous consent to submit.

Mr. STEARNS. Without objection, so ordered.

[The information follows:]

February 9, 2011

Medical Treatment, Out of Reach

By ANDREW POLLACK

Late last year, Biosensors International, a medical device company, shut down its operation in Southern California, which had once housed 90 people, including the company's top executives and researchers.

The reason, executives say, was that it would take too long to get its new cardiac stent approved by the Food and Drug Administration.

"It's available all over the world, including Mexico and Canada, but not in the United States," said the chief executive, Jeffrey B. Jump, an American who runs the company from Switzerland. "We decided, let's spend our money in China, Brazil, India, Europe."

Medical device industry executives and investors are complaining vociferously these days that the industry's competitive edge in the United States and overseas is being jeopardized by a heightened regulatory scrutiny.

The F.D.A., they and others say, appears to be reacting to criticism that its approvals for some products had been lax, leading to a spate of recalls of some unsafe medical devices, like implanted defibrillators and hip replacements.

Now, executives of device companies say the F.D.A. has gone too far in flexing its regulatory muscle, and they worry that a slower, tougher approval process in a weakened economy could chill investments and cripple innovation.

In addition, they say that American patients are being deprived of the latest technology because companies routinely seek approval for new devices in Europe first. For instance, heart valves that can be installed through a catheter instead of open-heart surgery have been available in Europe since 2007 but will not be available in the United States until late this year at the earliest.

"Ten years from now, we'll all get on planes and fly somewhere to get treated," said Jonathan MacQuitty, a Silicon Valley venture capitalist with Abingworth Management.

Marti Conger, a business consultant in Benicia, Calif., already has. She went to England in October 2009 to get an implant of a new artificial disk for her spine developed by Spinal Kinetics of Sunnyvale, Calif.

"Sunnyvale is 40 miles south of my house," said Ms. Conger, who has become an advocate for faster device approvals in the United States. "I had to go to England to get my surgery."

Stenum Spine Hospital in Germany has performed disk surgery on 1,000 Americans over the last eight years, said Jim Rider, the hospital's American marketing agent.

Acknowledging industry concerns, the F.D.A. on Tuesday proposed creating an "innovation pathway" aimed at speeding regulatory reviews of a small number of groundbreaking devices. And last month the agency announced measures it said would make the regulatory process more predictable for the vast majority of devices.

"A consistent and predictable review process will stimulate investment here at home and keep jobs from going overseas," Dr. Jeffery Shuren, the director of the agency's medical device division, told reporters.

But Dr. Shuren said the F.D.A. would not relax its standards, arguing that Europe's system might be too lax. He said that a breast implant, a lung sealant and an implant for elbow fractures were approved in Europe but not in the United States, and then had to be taken off the market in Europe for safety reasons.

"We don't use our people as guinea pigs in the U.S.," he said

Medical device executives said they welcomed the steps, but continued to express concerns. Consumer advocates, like Dr. Sidney Wolfe of Public Citizen, however, said that device regulation was already much less stringent than for drugs and that the F.D.A. was caving in to industry demands rather than ensuring consumer safety.

Dr. Charles Rosen, a spine surgeon who is also president of the Association for Medical Ethics, said that the newest devices were not always best. He said he had at least 50 patients who had suffered serious problems from an older artificial disk. Many of those patients, he said, had gone to Europe to get them before they were available in the United States.

Just since November, three reports — two sponsored by device industry trade groups and one conducted by the consulting firm PricewaterhouseCoopers — have raised concerns about the F.D.A. approval process. One report found that the rate of recalls in Europe was similar to that in the United States, suggesting faster approvals overseas were not hurting patients.

The complaints are driven in part by financial pressures. Venture capitalists, because of the financial crisis and their own poor returns, have less money and need quicker returns on their investments from the companies they back.

Bigger device companies also complain about the F.D.A., but not as much as struggling start-ups. "The F.D.A. is asking for larger trials, more thoughtful trials, all in the interest of the American public," said Dr. Stephen N. Oesterle, senior vice president for medicine and technology at Medtronic.

To be sure, the United States remains the clear world leader in medical device innovation, according to the report by PricewaterhouseCoopers. Some 32 of the 46 medical technology companies with annual sales exceeding $1 billion are based in the United States, the report said.

Still, the report said the United States' lead was slipping.

Device companies have been seeking early approval in Europe for years because it is easier. In Europe, a device must be shown to be safe, while in the United States it must also be shown to be effective in treating a disease or condition. And European approvals are handled by third parties, not a powerful central agency like the F.D.A.

But numerous device executives and venture capitalists said the F.D.A. has tightened regulatory oversight in the last couple of years. Not only does it take longer to get approval but it can take months or years to even begin a clinical trial necessary to gain approval.

Disc Dynamics made seven proposals over three years but could not get clearance from the F.D.A. to conduct a trial of its gel for spine repair, said David Stassen, managing partner of Split Rock Partners, a venture firm that backed the company. "It got to the point where the company just ran out of cash," Mr. Stassen said. Disc Dynamics was shut down last year after an investment of about $65 million.

Dr. Shuren of the F.D.A. said the agency had concerns from preliminary studies that the material in the gel could cause cancer and that the gel would come out of the disk, requiring a new operation.

Some companies and investors are even contemplating forgoing the American market completely.

"We never intend to spend a nickel in the United States for clinical trials," said William Starling, a venture capitalist who also runs Synecor, a device company incubator in North Carolina.

Mr. Starling is an investor in Spinal Kinetics, whose artificial disk was implanted in Ms. Conger

in England.

The company began working with both the F.D.A. and European regulators in early 2005. It won approval in Europe in 2007 after testing its device in 30 patients and spending $4 million. Since then, thousands of the disks have been implanted.

Only last May did it receive approval for a final trial for F.D.A. approval that would involve about 250 patients. But hard-pressed investors are not willing for now to put up the $50 million or so the trial would cost, Mr. Starling said.

In the meantime, Spinal Kinetics is moving its manufacturing to Germany and has already laid off 20 people in Silicon Valley. One reason for the move, Mr. Starling said, was that some countries in Asia and Latin America allowed use of devices that have been approved in the country in which they are made. So moving manufacturing out of the United States opens up those markets.

Totally forsaking the lucrative American market could be difficult. While approval in Europe is easier, health care systems there tend to spend less on medical devices. Even if a device were approved, doctors in Europe might not use it if there was not enough data proving it really works.

Some companies, however, are trying to generate some sales in Europe in an effort to be acquired by a bigger company, which could then afford to deal with the F.D.A.

Dr. Shuren of the F.D.A. said in an interview that there had been "no conscious effort" to make device approvals tougher. "We are dealing with increasingly more complex devices coming to market," he said.

But numerous executives say agency reviewers seem to be more cautious as Congress and others criticize the agency for being too lenient. Critics cited two recent examples: the DePuy hip implant recalled last year and an instance in which top agency officials approved a knee repair implant, made by ReGen Biologics, over the strenuous objections of their scientific reviewers.

Pharmaceutical executives are also complaining about how tough the F.D.A. has become. But they are not forsaking the American market, in part because there is not a big disparity in the regulatory system for drugs between the United States and Europe.

Some figures bear out a toughening in devices. The F.D.A. last year granted 19 premarket approvals — the type of clearance required for the most highly regulated devices — down from 48 in 2000.

The average time to win an approval through the less stringent 510(k) pathway, which is used for most devices, rose to 116 days in fiscal year 2008 from 97 days in fiscal year 2002. Agency figures show there have been increases in the proportion of applications sent back for questioning.

Investment by American venture capitalists in the medical device sector has fallen 37 percent since 2007 to $2.3 billion last year, according to the MoneyTree survey from PwC, the National Venture Capital Association and Thomson Reuters. That is steeper than the 27 percent drop for all venture capital investing.

Last year, total venture capital investing increased 19 percent while investment in medical devices fell 9 percent.

Mr. TERRY. Biosensors International, a medical device company, shut its operation in southern California, which had once housed 90 people, 90 lost jobs. The CEO is moving the manufacturing to Europe and says their stent "is available all over the world including Mexico and Canada but not in the United States. We decided, let's spend our money in China, Brazil, India and Europe." It is disappointing to hear the CEO's statement.

We hear later in the article a quote from a capital venture company who says, "Ten years from now, we'll all get on planes and fly somewhere else to get treated." That is a true indictment of our FDA's inability to timely approve medical devices, and I would like to see us, the United States, continue to be the world leaders in technology development. Yield back.

Mr. STEARNS. I thank the gentleman.

The gentlelady from Tennessee, Ms. Blackburn, is recognized for 1 minute.

OPENING STATEMENT OF HON. MARSHA BLACKBURN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Mrs. BLACKBURN. Thank you, Mr. Chairman, and welcome to all of our witnesses. We are grateful that you would take your time and be here with us today.

Continuing on the theme of making these innovations, having the innovations here, I think it is important for us to realize that 40 percent of the global medical technology industry is here in the United States, and it represents about 2 million U.S. jobs. Where I am from in Tennessee, we have about 10,000 individuals who are employed in the medical device industry and the wages and earnings are about 40 percent higher than the average earnings. So when you look at it from an issue of keeping those jobs here, it is vitally important.

When you look at the fact that we are in a 21st century creative economy and innovation, intellectual property and protecting that is vital to jobs retention. We want to make certain that FDA is responsive and responsive in a timely manner.

Welcome to the hearing, and I look forward to questions.

Mr. STEARNS. I thank the gentlelady.

The ranking member from California, Mr. Waxman, is recognized for 5 minutes.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you, Mr. Chairman, for holding this important hearing today.

I think we can all agree it is critically important that innovation in the medical device industry is vibrant and healthy, and that patients have access to the best and newest technological advances. If FDA is unnecessarily impeding technological advances that improve the lives of patients, we should all be united in doing whatever it takes to remove these unnecessary regulatory barriers to public health.

But we cannot have a conversation about the impact of regulations and policies at FDA have on patient access and innovation without talking about the importance of ensuring the safety and effectiveness of medical devices. We should not forget that that is the fundamental mission of FDA.

Practically every month, there is a new report in the papers about horrific patient suffering from dangerous medical devices. Last year, the New York Times revealed that radiation machines have killed and disfigured patients. The Subcommittee on Health held a hearing on the issue and heard from a father whose son was killed by an overdose from radiation therapy. We learned this year that malfunctioning linear accelerators have left patients nearly comatose and unable to speak, eat or walk.

Just last month, the New York Times reported on the suffering caused by faulty metal-on-metal hip implants. According to the Times, patients were promised these hips would last longer and enable more activity. About half a million patients got these devices. Now they are being recalled due to high rates of failure and patients have suffered severe health effects and have been forced to undergo surgery to replace the defective devices.

And these are just the most recent examples. We have also heard about problems with implantable heart devices that shocked patients and led to at least 12 deaths. Implantable defibrillators made by another company were failing for years before the manufacturer told anyone.

Our focus in this committee should be on how we can strengthen our device laws to protect patients from these grievous harms. Yet I fear that this is not the committee's goal today. Instead of strengthening our device laws, Republican members have proposed radical changes to our device laws that could further imperil patients. That is exactly the wrong direction for us to take.

We will hear testimony today that FDA is imposing new restrictions to innovation. Device industry advocates often refer to two industry-funded reports, one conducted by Dr. Josh Makower and one by the California Healthcare Institute, that they say show that FDA is unduly slow, burdensome and unpredictable. Yet neither of these studies, as Ms. DeGette pointed out, was published in a peer-reviewed journal, and both of these studies were funded by and conducted for industry advocates. Because of the lack of independent validation of these reports, I asked my staff to request that the editors of our Nation's top medical journals, one of whom is a witness today, examine the methodology of these two industry papers. All three editors we asked agreed to participate.

As our witness will describe today, there are serious methodological flaws in both studies—biased samples, small sample size and botched statistical analysis, just to name a few—rendering them essentially useless as part of any discussion of FDA's regulatory system. None of the editors felt that the methodology of these studies was worthy of publication in a peer-reviewed journal.

We will also hear today from six witnesses who will express their concerns that the FDA's device regulatory system is depriving patients of new and potentially life-saving devices, inhibiting innovation, and costing Americans jobs. FDA can and should do better in many of these cases. But we can't legislate by anecdote.

We need to ask why unsafe devices have gotten onto the market and harmed so many patients. Then we need to explore how we can strengthen the FDA review process to protect patients from these risks. The soon-to-be-released recommendations from the Institute of Medicine could provide a roadmap for how to improve FDA's regulatory oversight of medical devices.

In order to have a flourishing and innovative American device industry that puts safe and effective devices on the market, we need to have a strong and well-resourced FDA. That is in the best interest of American patients. It is also in the interest of the device industry itself. If patients lose confidence in the FDA, they lose confidence in the industries it regulates as well.

This is an issue that can and should be bipartisan. I look forward to hearing from our witnesses and to working with my colleagues on this important matter.

[The prepared statement of Mr. Waxman follows:]

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED TWELFTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115

Majority (202) 225-2927
Minority (202) 225-3641

Opening Statement of Rep. Henry A. Waxman
Ranking Member, Committee on Energy and Commerce
"Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs"
Subcommittee on Oversight and Investigations
July 20, 2011

Thank you, Chairman Stearns, for holding this important hearing today.

I think we can all agree it is critically important that innovation in the medical device industry is vibrant and healthy, and that patients have access to the best and newest technological advances. If FDA is unnecessarily impeding technological advances that improve the lives of patients, we should all be united in doing whatever it takes to remove these unnecessary regulatory barriers to public health

But we cannot have a conversation about the impact regulations and policies at FDA have on patient access and innovation without talking about the importance of ensuring the safety and effectiveness of medical devices. We should not forget that that is the fundamental mission of FDA.

Practically every month, there is a new report in the papers about horrific patient suffering from dangerous medical devices. Last year, *The New York Times* revealed that radiation machines have killed and disfigured patients. The Subcommittee on Health held a hearing on the issue and heard from a father whose son was killed by an overdose from radiation therapy. We learned this year that malfunctioning linear accelerators have left patients nearly comatose and unable to speak, eat, or walk.

Just last month, *The New York Times* reported on the suffering caused by faulty metal-on-metal hip implants. According to the *Times*, patients were promised these hips would last longer and enable more activity. About half a million patients got these devices. Now, they are being recalled due to high rates of failure and patients have suffered severe health effects and have been forced to undergo surgery to replace the defective devices.

And these are just the most recent examples. We've also heard about problems with implantable heart devices that shocked patients and led to at least 12 deaths. Implantable defibrillators made by another company were failing for years before the manufacturer told anyone.

Our focus in this Committee should be on how we can strengthen our device laws to protect patients from these grievous harms. Yet I fear that this is not the Committee's goal today. Instead of strengthening our device laws, Republican members have proposed radical changes to our device laws that could further imperil patients.

That is exactly the wrong direction for us to take.

We will hear testimony today that FDA is imposing new restrictions to innovation. Device industry advocates often refer to two industry-funded reports – one conducted by Dr. Josh Makower and one by the California Health Institute – that they say show that FDA is unduly slow, burdensome, and unpredictable.

Yet neither of these studies was published in a peer reviewed journal, and both of these studies were funded by and conducted for industry advocates. Because of the lack of independent validation for these reports, I asked my staff to request that the editors of our nation's top medical journals, one of whom is a witness today, examine the methodology of these two industry papers. All three editors we asked agreed to participate.

As our witness will describe today, there are serious methodological flaws in both studies – biased samples, small sample size, and botched statistical analysis, just to name a few – rendering them essentially useless as part of any discussion of FDA's regulatory system. None of the editors felt that the methodology of these studies was worthy of publication in a peer-reviewed journal.

We will also hear today from six witnesses who will express their concerns that the FDA's device regulatory system is depriving patients of new and potentially life-saving devices, inhibiting innovation, and costing Americans jobs.

FDA can and should do better in many of these cases. But we can't legislate by anecdote.

We need to ask why unsafe devices have gotten onto the market and harmed so many patients. Then we need to explore how we can strengthen the FDA review process to protect patients from these risks. The soon-to-be-released recommendations from the Institute of Medicine could provide a roadmap for how to improve FDA's regulatory oversight of medical devices.

In order to have a flourishing and innovative American device industry that puts safe and effective devices on the market, we need to have a strong and well-resourced FDA. That is in the best interest of American patients – but it is also in the interest of the device industry itself. If patients lose confidence in the FDA, they lose confidence in the industries it regulates as well.

This is an issue that can and should be bipartisan. I look forward to hearing from our witnesses today and to working with my colleagues on this important matter.

Mr. STEARNS. I thank the gentleman.

Let me say, we have seven witnesses, not six, and we welcome all seven witnesses to our hearing, and I call attention to the bio of each of these witnesses. If members will take the time to read that, I won't have to go through all seven.

Let me address all of you. You are aware that the committee is holding an investigative hearing, and when doing so has the practice of taking testimony under oath. Do any of you object to taking testimony under oath? No? The chair then advises you that under the rules of the House and the rules of the committee, you are entitled to be advised by counsel. Do you desire to be advised by counsel during your testimony today? In that case, if you would please rise and raise your right hand, I will swear you in.

[Witnesses sworn.]

Mr. STEARNS. You are now under oath and subject to the penalties set forth in Title XVIII, section 1001 of the United States Code. We welcome your 5-minute opening statement, and your written statement will be part of the record.

Dr. Fischell, we will start with you. Welcome.

TESTIMONY OF ROBERT E. FISCHELL, CHAIRMAN AND CEO, FISCHELL BIOMEDICAL LLC; CAROL MURPHY, PATIENT; MARTI CONGER, PATIENT AND PATIENT ADVOCATE; PAM K. SAGAN, PATIENT; MICHAEL MANDEL, CHIEF ECONOMIC STRATEGIST, PROGRESSIVE POLICY INSTITUTE; SEAN IANCHULEV, CHIEF MEDICAL OFFICER, TRANSCEND MEDICAL, INC.; AND GREGORY D. CURFMAN, EXECUTIVE EDITOR, NEW ENGLAND JOURNAL OF MEDICINE

TESTIMONY OF ROBERT E. FISCHELL

Mr. FISCHELL. Chairman Stearns, Ranking Member DeGette, members of the subcommittee. My name is Robert Fischell, and I am pleased to testify today about an issue of great importance to me, to patients, to physicians and to the American public.

For more than four decades of my 82 years, I have dedicated my life to inventing and developing novel medical technologies including an implantable insulin pump for diabetics, heart pacemakers, implantable defibrillators, and co-inventing about 10 million of the heart stents that have improved health and saved lives of patients in the United States and throughout the world. I have personally been the inventor or co-inventor on more than 10 medical devices including a new external device that is effective in eliminating the pain of migraine headaches, which device is here in front of me on this table.

These technologies have also spurred tens of thousands of jobs in this country and resulted in billions of dollars in U.S. exports to other countries that value our American medical devices. Unfortunately, the environment that exists at FDA's Center for Devices and Radiological Health over the past few years is the worst that I have experienced in my 42-year career involving medical technologies.

Given the success I have enjoyed over the years, some might ask why am bothering to testify today. It is certainly not in pursuit of money. I have enough to live pretty well. I am here today because

of the millions of patients and physicians who are searching for therapies to improve the human condition. Unfortunately, it is not technology, science, ingenuity or the economy that is standing in the way of success in developing new medical technologies. In my opinion, it is today the FDA. As a strong supporter of President Obama and his policies, that is not easy for me to say.

Prior to 2008, CDRH division was demanding safety and efficacy for the many new medical devices that I had invented. At that time, they were reasonable in allowing clearance of devices that showed safety and efficacy. CDRH demonstrated the ability to properly weigh the benefits and risks of new medical devices as part of the premarket review process. CDRH leadership understood that medical devices may have some risks, but corresponding benefits that patients realized with the therapy they provided were worth the risk associated with such devices.

Over the past few years, I have personally been aware of many instances where product clearances were denied or significantly delayed by CDRH when the patient benefit clearly outweighed any potential risk to the patient. One example of this is a device that I invented that relieves the pain of migraine headache with no serious side effects, this device right here. That device was not approved by CDRH even after the clinical trial proved safety and efficacy. A somewhat trivial example is a small plastic valve that I have in my hand that could open or close to allow liquid to flow, and had its approval delayed by over a year when it had already been approved for regular use in other equipment.

The failure of the current CDRH to efficiently and effectively review medical devices is a serious problem for the citizens of the United States. Many published reports suggest that patients are being forced to travel outside the United States for therapies that were developed here. Even worse, many patients do not have the resources to travel abroad and are forced to suffer, waiting desperately for FDA to clear or approve therapies that in some cases have already been available for years outside the United States.

Beyond the adverse impact FDA is having on patient care, it is weakening the U.S. leadership position in medical technology innovation, and as a result, hurting our economy. As someone who has enjoyed success in this industry, I have been proactive in trying to assist the innovators, scientists and engineers of tomorrow to be in this field. I recently established the Fischell Department of Bioengineering and the Fischell Institute for Medical Devices at the University of Maryland. Today, I am truly concerned for those scientists, engineers and innovators who study there who are about to embark on their careers. If I were to be starting out today, I would likely be unable to make the contribution to patients' lives that I have made over the past 40-plus years because I would be unable to raise the funding or endure the delays that exist with the current regulatory environment at CDRH.

In dealing with the FDA today, the reviewers appear to be slowing down or totally denying clearances for valuable medical devices that would be of great benefit for patients in the United States. By doing this, they are proud of being so conservative. I mean, look how good I am, I am so conservative, I am not even going to approve it. I am aware of examples where reviewers have changed

the requirements for companies during the premarket review process with no credible evidence supporting the moving goalposts.

One such example has recently occurred with a device that I coinvented that improves the treatment for epilepsy using a tiny electrical stimulator that I have here.

The inability for reviewers to be held accountable for their changing standards and increased risk aversion is something Congress and undoubtedly this committee must address if we are to improve patient care in this country and promote innovation and jumpstart our economy. While it may be difficult to legislate culture and restore the collaborative, reasonable and effective CDRH that existed back in 2008, I urge this committee to try. Patients, physicians, innovators and the American public are counting on you to step up and restore a reasonable and predictable CDRH that appropriately balances risks and benefits, works collaboratively with industry and understands that unnecessarily denying——

Mr. STEARNS. Dr. Fischell, I need you to summarize.

Mr. FISCHELL. Two sentences.

Mr. STEARNS. Good. OK.

Mr. FISCHELL [continuing]. Access to medical therapy means that FDA is failing in its primary mission, which is to protect patients but also to allow clearance for devices to relieve pain and suffering that many patients would otherwise have to endure. Thank you.

[The prepared statement of Mr. Fischell follows:]

TESTIMONY OF DR. ROBERT E. FISCHELL

before the

HOUSE ENERGY AND COMMERCE COMMITTEE SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs

July 20, 2011

Chairman Stearns, Ranking Member DeGette, Members of the Subcommittee. My name is Robert Fischell and I am pleased to testify today about an issue of great importance to me, to patients, to physicians and the American public. For more than four decades I have dedicated my life to developing novel medical technologies, including an implantable insulin pump for diabetics, heart pacemakers, implantable defibrillators, and more than 10 million heart stents that have improved health and saved the lives of patients in the USA and throughout the world. I have personally been an inventor or co-inventor of more than ten medical devices including a new external device that is effective in eliminating the pain of migraine headaches. These technologies have also spurred tens of thousands of jobs in this country and have resulted in billions of dollars in US exports to other countries that value American medical devices.

Unfortunately, the environment that exists at FDA's Center for Devices and Radiological Health (CDRH) over the past few years is the worst I have experienced in my 42 year career innovating medical technologies. Given the success I have enjoyed over the years, some would ask why I am even bothering testifying today. It certainly is not in pursuit of money, I have enough to live very well. I am here today because of the millions of patients and physicians who are searching for therapies to improve the human condition. Unfortunately, it is not technology, science, ingenuity or the economy that is standing in the way of success in developing new medical technologies. It is the FDA. As a strong supporter of President Obama, this is not easy for me to say, but it is the truth.

Prior to 2008, CDRH division was demanding of safety and efficacy for the many new medical devices that I have invented. At that time they were reasonable in allowing clearance of devices that showed safety and efficacy. CDRH demonstrated the ability to properly weigh the benefits and risks of new medical devices as part of the premarket review process. CDRH leadership understood that medical devices may have some risks, but the corresponding benefits that patients realized with the therapy they provided were worth the risk associated with such devices.

Over the past few years I have personally been aware of many instances where product clearances were denied or significantly delayed by CDRH when the patient benefit clearly outweighed any potential risk to the patient. One example of this is a device that I invented that relieves the pain of migraine headache with no serious adverse effects. That device was not approved by CDRH even after the clinical trial proved safety and efficacy. Another example is an implantable heart defibrillator that included the ability to prevent death from a heart attack where CDRH stopped that company's ability to evaluate that urgently needed product even though the device would begin its study by merely recording data as to how heart attacks can be detected at the earliest possible moment. A somewhat trivial example is a small plastic valve that could open or close to allow liquid to flow that had its approval delayed by more than a year even after that valve was already approved by CDRH for other uses.

The failure of the current CDRH to efficiently and effectively review medical devices is a serious problem for the citizens of the USA. Many published reports suggest

that patients are being forced to travel outside the US for therapies that were developed in this country. Even worse, many patients do not have the resources to travel abroad and are forced to suffer, waiting desperately for FDA to clear or approve therapies that in some cases have been available years before they get approved in the US.

Beyond the adverse impact FDA is having on patient care, it is weakening the US leadership position in medical technology innovation and as a result, our economy. As someone who has enjoyed success in the medical device industry, I have been proactive in trying to assist the innovators, scientists and engineers of tomorrow. In addition to working on medical devices at the Johns Hopkins University, Applied Physics Laboratory for more than 20 years, I recently established the Fischell Department of Bioengineering and the Institute for Medical Devices at the University of Maryland. Today, I am truly concerned for the scientists, engineers and innovators about to embark on their careers. If I were to be starting out today, I would likely be unable to make the contribution to patient care I have made over the past 40+ years because I would be unable to raise the funding or endure the delays that exist with the current regulatory environment at FDA.

In dealing with the FDA today, the reviewers appear to be slowing down or totally denying clearances for valuable medical devices that would be of great benefit for patients in the US. By doing this they are proud of being really conservative. I am aware of examples where reviewers have changed the requirements for companies *during* the premarket review process with no credible evidence supporting the moving goal posts.

One such example has recently occurred with a device that I co-invented that improves the treatment for epilepsy using a tiny electrical stimulator implanted into the patient's cranial bone.

The inability for reviewers to be held accountable for their changing standards and increased risk-aversion is something Congress must address if we are to improve patient care, promote innovation and jumpstart our economy. While it may be difficult to legislate culture and restore the collaborative, reasonable and effective CDRH that existed a few years ago, I urge you to try. Patients, physicians, innovators and the American public are counting on you to step up and restore a reasonable and predictable CDRH that appropriately balances risks and benefits, works collaboratively with industry and understands that unnecessarily denying patients access to medical therapies means that FDA is failing in it's primary mission which is to protect patients but also to allow clearance for devices to relieve the pain and suffering that many patient's would otherwise have to endure.

Thank you.

Mr. STEARNS. Ms. Murphy, welcome.

TESTIMONY OF CAROL MURPHY

Ms. MURPHY. Thank you. Good morning. I am Carol Murphy.

I have been a migraine sufferer for 40 years. I have three to four aura migraines a week. I have been through beta blockers, antidepressants, anti-seizures, abortive medications. When you have done that, you go on to the next step, so I have had occipital blocks, I had steroidals, cervical blocks, I have had Botox with minimum success.

At Michigan Head Pain and Neurological Clinic, once you turn 60 years old, you don't fit any of the medical protocols for migraine medicine and therefore they left me with the narcotic oxycodone to take care of a migraine headache, and that was it.

I finally got into the trial program at Ohio State with the transcranial magnetic stimulator, TMS. I was told to put the device on my head, activate it twice during an aura. When I did that, the aura cycle kept going but at the end of the aura when the pain should have started, it didn't. The blood vessels did not fill up. There was no pain. There was no headache. For 9 months, I lived like a normal person, and then in June of 2006, Ohio State took it back because it was going to go through the FDA process for approval. Give us 9 months, give us a year, Carol. Yes. It is now June of 2011—July of 2011. Where is my machine? That is in England. That is not here. I can't get it here.

A lot of people think that a migraine is a headache. It isn't. When blood vessels swell in the brain, every part of your body can be affected. For me, my feet and legs get so cold that there is absolutely no way for me to sleep so going to bed and sleeping it off doesn't work. And there is no way of warming those legs until after the migraine stops. When I take OxyContin, it dulls the pain but it doesn't break the migraine cycle. With the TMS, no headache because the blood vessels weren't dilated.

With migraines, I also experience urinary and bowel problems. By the second day, I have abdominal pain. I also have problems concentrating. The thoughts in my head are clear but the words coming out of my mouth sometimes are not right or they just don't come out at all. This doesn't happen with the TMS because we don't have the dilation of the blood vessels.

As I get older, falling becomes a major problem for me, and my left leg drags during a migraine. So I need to be more careful. I need to have the good balance. And with the TMS, again, we don't have the lagging of the left foot.

Now I live my life between a rock and a hard place. I can take the medication, I can deal with the fact that it is addictive or I can crawl up in my little hole and stay there until it is over. Either way, that is not quality of life. I want my device back. I will go to England to get it. I will rob Peter to pay Paul to get there because for me, it is a quality-of-life factor.

I want to look forward to a life without any pain. I want to know that I am not going to wait until 3 or 4 or 5 years for the FDA to turn around and approve this machine.

There are millions of migraine sufferers. Everyone has their own story. I am one that medication just doesn't work for. We as Ameri-

cans should not have to go to England to get a piece of machinery that I know that I used 5 years ago safely. This is a product that was made in America, by Americans, but obviously not for Americans. How long do we have to wait? Five years is a long time. How many more years? How many more migraines am I going to go through if I am going to sit and wait for the FDA to approve this product?

Thank you for your consideration and time.

[The prepared statement of Ms. Murphy follows:]

Carol Murphy
Patient

Testimony for the Subcommittee on Oversight and Investigations

My name is Carol Murphy. I have had migraine headaches for over 40 years. Unfortunately I am one of those people for whom medication was far from successful. Once you have progressed through the beta blockers, anti depressants, anti seizures and abortive medications, you become willing to try more aggressive treatments. I have done occipital blocks, which causes scar tissue and the possibility of worsening headaches, and I have had steroidal cervical blocks and Botox with minimal success.

Michigan Head Pain and Neurological Clinic was able to designed a regiment for me that kept me out of the emergency rooms and functioning most of the time, but that all changed in 2005 when I turned 60. Just another milestone I thought, but for migraine sufferers, it becomes a traumatic age. I no longer fit into Michigan's protocols for migraine medications and so they would not allow me to continue with any of the medications I was on. Instead, " stroke risk" was stamped on my forehead. So I quickly had a "stroke assessment" done which proved that everything was in normal limits but "protocols" outweighed that assessment and I was left with nothing more than the narcotic pain killer oxycodone. Oxycodone numbs the pain but nothing to break the headache cycle, and with 3-4 aura migraines a week, my life was going done hill fast.

When I got into the program at Ohio State with the Transcranial Magnetic Stimulator, I had little expectations of it working. I was told to put the devise on my head and activate it twice during the aura. When I used the devise, the aura finished it's cycle, but the blood vessels in the

brain never filled with blood-- therefore no pain. For 9 months I had a normal life. If I had promised to do something on a particular day, I could! I never left the house without my devise. If my car was going to be more than 15 minutes away from me, I carried my devise with me. My life had turned around- I could do anything, any time I wanted to! You could say I was living life again.

In June of 2006, Ohio State took back the TMS(Transcranial Magnetic Stimulator), so it could go to the FDA. It is now July 2011 and where is my devise? In England!

In many ways, I am not the classic migraine sufferer. When people think about a migraine, the picture they see is of someone in a dark room, rolled up in a ball, vomiting. That is not me. When the blood vessels in your head expand, any part of your body can be effected. My feet and legs get so cold there is no way I can sleep. I call it bone cold because there is no way of warming them until the migraine lets up. Oxy(oxycodone) numbs pain , but it does not break the cycle of a migraine. With the TMS, the blood vessels never dilated- no cold feet. Sleep!

Although vomiting is not a problem, I do have urinary and bowel problems. By day two, the abdominal migraine starts. I walk around holding my lower abdomen as if I had just had surgery. Again, no dilated blood vessels, no abdominal pain.

But for me, the more serious problem is neurological. I call it "MY no noun days". If the headache lasts 2-3 days, then there are "No adjective days" as well. The thoughts in my head are clear, but the words coming out of my mouth are jumbled or nonexistent. Sometimes it's just easier to not try to communicate, but I still work. It's hard to be professional when you are constantly saying "Let me start

over." With the TMS, none of this happens.

As I age, falling becomes more of a factor. During a migraine, my left foot drags. With my balance just off a little because my ears feel full, catching my toe is really dangerous. Lack of balance and a "foot drop" gets more critical with each year. With the TMS, this also doesn't happen.

Now I live my life between a rock and a hard place. I can take the narcotic OXYI and be at risk for the addiction that can come with it and be faced with the possibility of having a stroke after an aura, or I can go without any medication and let the pain tear my body down. Some days I want a life and just take the medication, but other days I just crawl into my hole and grin and bear it, so as not to feel drugged all the time. I want my machine back!! I want to look forward to a quality of life free of pain. Most people can't say they can go back in time, but I can. If I had that TMS devise, health wise I could go back five years to a time when my life was free of pain. Five years is a long time to wait!

There are millions of migraine sufferers out there. They all have their own story to tell. Most everyone knows someone who has migraines. Drugs are not always the answer. We, as Americans, should not have to go to England to get medical equipment to help live a normal life. This is a product made in America, by Americans, but not for use by Americans. We waited five years for FDA approval. How many more years is it going to take to bring us up to UK standards in medical equipment?

Mr. STEARNS. Ms. Murphy, that is very compelling. Thank you. Ms. Conger, you are recognized for 5 minutes.

TESTIMONY OF MARTI CONGER

Ms. CONGER. And I timed the 5 minutes, practicing on the airplane.

Hello, and I thank you very much for the invitation to testify. I am a spine patient and a very angry one. I became livid when I figured out that my government was the main barrier between me and the best solution for my spine problem.

I am here today as an advocate for the millions of U.S. patients like me who are needlessly suffering, deteriorating and sometimes dying while they wait for the FDA to approve medical devices they desperately need, devices that are often already in successful use in other countries.

Briefly, a little about me. My TOS specialist identified my cervical spine issue in 2006 and quickly sent me to University of California San Francisco Spine Clinic to Dr. Dean Child, who had been involved in cervical spine artificial disc trials, clinical trials.

Now, I have been dealing with multiple life-altering health issues, and since I can't take narcotics or opiates, I was already physically and mentally drained from chronic pain and raging paresthesia. If you want to imagine that, just walk around barefooted on a bristle brush, and that is paresthesia in your feet.

My neurosurgeon's—my surgeon's diagnosis just had me reeling. What else can go wrong? I already had this long list of deals. But he immediately started educating me. After he reviewed my films in detail, we discussed my options, the benefits and consequences, and in my case, my choices were, first, do nothing, wait for quadriplegia in the next couple of years, or have fusions, which I later learned meant I would likely have chronic pain in my neck and possibly have cervical fusion in the future. The third choice, wait a couple of months for an artificial cervical disc in the FDA approval pipeline, one widely used and successfully in Europe since 2003.

While I waited for device approval, my spine degenerated to the point that my doctor and I feared I was in serious danger. All my limbs were numb. My continence was an issue. My balance and my grip were unreliable. I was a prisoner in my own house for fear of going outside and having a paralyzing accident, and I depended on everyone else to take care of my needs. I knew I couldn't living this way safely but I was not having fusions. Nor could I believe the newer clinical cervical device technology which my doctor and I felt was best for my problems were made 40 miles south of my house and I could not get them installed in my Nation. Forty miles from my house. By the way, those jobs have disappeared to Europe because European countries will sometimes say, if you don't have approval in the United States or your home country, country of manufacture, you can't sell them here. So they moved all those jobs, those $160,000 to $100,000 jobs to Germany. Yet these devices were in successful use in Europe and elsewhere.

My only option to get the best solution for me was for me to go abroad. It took research and months of fundraising. We drained our savings, what little we had. We accepted $5,000 in gifts from

friends and family. I stripped my life insurance policy of cash value. We incurred credit card debt, and my 75-year-old husband had to return to full time, and he has been working since.

Finally, I had my two-level ADR surgery in 2009 at the Spine Clinic in England. My pain relief was immediate, and my discs are functioning flawlessly. My U.S. neurosurgeon is delighted. He does my follow-up.

And what about all the other—so I got the best solution for me but it shouldn't have taken all my limited energy and money to get them. What about all the other Marti Congers in this country, people waiting for access to medical devices that already have foreign approvals and years of track record. I know, because I receive calls and emails every week from spine patients from auto mechanics to engineers to cardiac surgeons. They want to know how they might get the treatment they need somewhere, somehow, because they are not going to do the procedure here. And what about all the other devices common in Europe and in Asia but bogged down in the FDA process. Products often invented here aren't available to U.S. patients for years after patients around the world already have them. It simply shouldn't be this way. It shouldn't.

I do appreciate, Mr. Stearns, that the agencies' challenges that they face right now from all directions. I appreciate their desire to protect people. However, our FDA needs to restart, reset their priorities back to patients' needs and away from political risk aversion. Patients are looking for reasonable assurance and timely approval or denial—not all devices make it—but absolute assurance, what seems to be the goal here, is impossible, impossible, because every human body is unique.

For products with strong track records, the FDA should leverage regulatory findings from other trusted countries and unions such as Japan, Australia, European Union and others, and put them into the marketplace or at a minimum fast-track them, then monitor—oK. Two sentences?

Mr. STEARNS. Just if you could wrap up.

Ms. CONGER. Yes. Monitor them in the marketplace. Requiring known devices to restart the approval process from the beginning when thousands of human already have them in their body is ludicrous. The sooner we act on these changes, the sooner U.S. patients will have access to the devices they need at a reasonable price instead of waiting 2 to 10 years to get the device here.

[The prepared statement of Ms. Conger follows:]

Written statement of:

Ms. Marti Conger, M.Ed.
Patient/Patient Advocate

Before the:

Subcommittee on Oversight and Investigations
of the House Energy and Commerce Committee
US House of Representatives

Hearing titled:

"Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation, and Jobs."

July 20, 2011

FDA Medical Device Regulation: Impact on American Patients, Innovation, and Jobs

It shouldn't be this way!

Thank you, Mr. Chairman and members of the Committee – my fellow citizens – for your invitation to testify about how the FDA approval process impacts patients and, therefore, medical device innovation and jobs.

My name is Marti Conger. I'm a spine patient, and a very angry one. Because of my experience, I've vowed to instigate changes in FDA practices to guarantee all US citizens equal access to the most current, successful medical technology which the doctor and patient agree is appropriate.

I became livid when I figured out that my government was the main barrier between me and the best solution for my spine problem. Worse, I'm just one of too many in this country with the same barrier.

I believe it's my civic duty to make things better for my fellow citizens who are also awaiting successful devices that are essential to their health and/or life sustainability. Specifically, I'm asking Congress to

> *require the FDA to accept the regulatory findings of products with strong track records from other trusted countries and unions (i.e., from Europe, Australia, Japan, and others), and put them into the marketplace or, at a minimum, "fast track" them. Then monitor the devices as they currently do in the marketplace.*

I came to testify as an advocate for the millions of US patients like me who are needlessly suffering, deteriorating, *and sometimes dying* while they wait for the FDA to approve the medical devices they desperately need; particularly Class III devices that are often already in successful use in other nations.

Let me tell you a bit about my story. Then I'll share the changes I'm working toward to resolving the problems US patients face relative to medical device access. I ask you to help me, because it shouldn't be this way!

A bit of my story

My thoracic outlet syndrome ("TOS") specialist identified a cervical spine issue in 2006, and quickly sent me to the UCSF Spine Clinic, to a neurosurgeon who'd been a participating physician in artificial cervical disc clinical trials.

I've been dealing with multiple, life-altering health issues and, since I can't take opiates or narcotics (or their substitutes), I was already physically and mentally drained from chronic pain and raging paresthesia.

My neurosurgeon's diagnosis had me reeling, but he immediately started educating me. After we reviewed my films in detail, we discussed my options and their benefits and consequences. In my case, my choices were to:

1. Do nothing and wait for quadriplegia in the next couple of years
2. Have fusions – which I later learned meant I'd likely still have chronic pain, and possibly have serial fusions in the future
3. Wait a couple of months for an artificial cervical disc in end of the FDA approval pipeline – one successfully used in multiple cervical spine levels in Europe since 2003

I did my research and chose artificial disc replacement ("ADR") over fusion because I wanted to:

- retain neck motion,
- avoid future serial fusions,
- avoid any cage or strap hardware which usually cause chronic pain, and
- have a two–four week recovery instead of the typical four–six months for fusions.

My neurosurgeon was willing to support my waiting until the FDA approved the artificial disc – with lots of restrictions on me, of course. Naively I thought, "How long could it take? There are already so many good ADR device options in regular use in Europe – including this one!"

Instead of a couple of months, the FDA took another 12 months to finish approving it. More bizarre was that they restricted the device to just one level and from kyphotic patients – which I'd become. Why? In other countries, this device has had years of success in multiple levels in thousands of patients, and is not restricted from kyphotic patients. Why does the FDA impose such restrictions when the manufacturers have data to refute them?

While I waited for device approval, my spine degenerated to the point that my neurosurgeon and I feared I was in serious danger: all of my limbs were numb, my continence was a huge issue, my balance and grip unreliable. I was nearly a prisoner in my home for fear of paralyzing accidents. I depended on others for everything but my most basic needs. I admit I refused my doctor's requests to reconsider fusion but I also knew I couldn't continue to safely live without treatment.

After much research, I changed my artificial disc choice to a newer technology that emulates the human disc and which had been available and successful outside the US since 2005. Since the device had been in the FDA process since 2006, I desperately searched for Spinal Kinetics' M6-C trials in the US, but the few that were open were limited to one level. I needed two, possibly three levels, which is approved and successful outside the US.

Nor could I believe that the newer cervical disc technology, which my doctor and I felt was best for my problems, were made forty (40) miles from my house and I couldn't get them here!!! Yet, they were widely available in Asia, Europe, and elsewhere. The only option to get the best devices for me was to go abroad.

It took research and months of fund raising. We drained what savings we had, accepted $5,000 in gifts from friends and family, stripped my life insurance policy of cash value, incurred credit card debt, and my then-75-year old husband had to return to work full time (and still does due to my health).

At last, I had my two-level ADR surgery in October 2009 with Nick Boeree at The Spine Clinic in southern England. My pain relief was immediate and my discs are functioning flawlessly. I had surgery on Wednesday, toured Winchester Cathedral on Sunday, and flew home a couple of days later. My US neurosurgeon is thrilled with the results, too, and does my follow-up.

I'd like to note that my surgery, done in a private hospital, cost less than half of what a like-surgery would typically cost in the US. Based on studies presented in previous hearings by Congressional Committees on this subject, I venture to say that much of the huge cost difference can be tracked directly to approval process delay expenses incurred by the manufacturer.

While I was blessed to get the best solution for me, I still say there is absolutely no reasonable justification for having to wait years and raise tens of thousands of dollars to get access to a successful, US-developed technology if our FDA approval process and our health insurer regulations worked for patients.

It shouldn't be that way!

And what about the other Marti Conger's in this country? For example, there are more than 200,000 spine fusions done on US patients every year when there are far better solutions available everywhere except the US. People are waiting for access to medical devices that already have CE-marking and years of track record. I know, because I receive calls and emails every week from other spine patients – from auto mechanics to

engineers to heart surgeons – who want to know how they might get the treatment they need … somewhere, somehow. It shouldn't be that way!

And what about all the other devices successful and widely used abroad but bogged in the FDA process – CoreValve heart valves, PFO devices for certain migraine patients, and the list goes on. Products, often invented here, aren't available to US patients for years after patients around the world have already had them. It shouldn't be that way!

The US was once the ultimate place to get superior medical treatment. Now, instead of being the first to benefit from our own medical technology advances, we're often the last and we're not benefiting from the delays. In sum:

- Patients with means are flocking to Europe for devices – frequently invented in the US – that are approved abroad or approved with unnecessary restrictions.
- Patients who can't scrape enough together to travel to get to more effective devices denied them by the FDA either: 1) succumb to archaic methods in-country, 2) do nothing, 3) degenerate beyond treatability, or 4) die waiting to get the right treatment.
- US inventors are more and more often choosing to forego the US market because of the onerous and often adversarial FDA approval process that costs millions more than the equally safe EU process.
- Fewer and fewer non-US inventors are willing to run the FDA gauntlet to gain product approval, further diminishing US access to new medical technologies. Those that do are simultaneously moving forward in Asia and Europe with their 4th and 5th generation of the same device which will likely never see the light of day in the US.

It shouldn't be that way!

Unfortunately, I'm one of many with the personal experience to prove it. The devices I traveled to England to receive have been available in Europe since 2005 with a strong track record, and are still years away from the marketplace in the US. It makes no sense that the FDA doesn't recognize data from other, trusted nations with robust regulatory systems.

Remember, there are people waiting for these devices! People who are dying, or failing beyond recovery, or not being able to live a normal life, draining all of their finances to get care until they receive the proper treatment.

With each inappropriate process decision or delay, there are real people who need solutions now; people like me, Rob, Christine, Patrick, Wayne, Linda, Victoria, Alexander ... It just shouldn't be that way!

FDA and skepticism

First we must recognize that the FDA's CDRH has been making a herculean effort to keep pace with an industry that's innovating exponentially – both technologically and scientifically. This requires huge changes in infrastructure, type of intellectual property, culture, and the will to make those changes at the speed required. While change isn't easy for any organization, change is necessary for the FDA and CDRH to give US patients more timely access to safe and effective new therapies. These changes are vital for the sake of US patients' health.

I do appreciate the challenges the agency faces – from all directions. I appreciate their need to protect patients. However, our FDA needs to re-set their priorities back to patients' needs and away from political "risk aversion."

I also acknowledge that the skepticism about new technologies is real. We've all heard enough FDA "fear fodder." For example:

- "We aren't going to use our people for guinea pigs."

  Be serious. No one – here or abroad – is serving as guinea pigs!
- "Non-US results aren't appropriate for the US market."

  Why? Both Europe and North America are ethnic melting pots.
- "Only the US can test products sufficiently to be sure they're right."

  The arrogance of "not invented here = not good enough" is causing US patients to wait much longer for successful products.
- "The CE-marking process is "easier [and therefore, not reliable]."

  Wrong! It only looks easier because the CE process is reliable, consistent, transparent, and reasonable and usually takes less time and money, which results in equally effective products and lower product costs.

What must change now

It's time for the agency and insurers to remove themselves from patient/doctor decisions. The ultimate decision about healthcare should be between a patient and their physician. We, the public, need the FDA to determine reasonable assurance of safety and efficacy. As a patient I don't expect, nor is it desirable for, the FDA to seek "absolute" assurance; it isn't feasible because every body is unique. The valuable time used to find the ever illusive "absolute" assurance often means that patients are denied product access or, when the product is finally approved, the cost is so high and/or insurers refuse to cover them that they're not accessible. Please, verify that the product will function as designed (which includes safety); then let the patient and doctor make the decision.

The FDA needs to accept the regulatory findings of products with strong track records from other trusted countries and unions (i.e., from Europe, Australia, Japan, and others), and put them into the marketplace or, at a minimum, "fast track" them. Then monitor them as they currently do in the marketplace.

If just "fast tracking," accept all of a manufacturer's scientific evidence collected from device pre-approval testing, trials, and actual market experience without bias or discrimination regardless which trusted nation in which the evidence was collected. For products with existing foreign approvals that required human trials, additional US human trials should be a last resort after all other evidence has been reviewed.

Nor should the agency place medically unfounded restrictions on devices – particularly when the manufacturer has evidence to refute the proposed restriction(s). For example, don't limit an artificial cervical disc to one level when the product is shown successful in multiple levels in the same patient.

The impact of "not-invented-here"

Eliminating the "not-invented-here" bias at the FDA applies most to scientific evidence; doing so is critical to making significant progress in getting successful products to the US market faster. What is important is the quality of the data – not where the data was collected.

Requiring known devices to restart the approval process is a waste of time and resources – and often costs patients' lives while they wait. The data from successful products approved outside of the US is a tool and support for the FDA's need for data to avoid risk.

By the time a US or EU manufacturer decides to bring their CE-marked product to the FDA, they already have more pre- and post-approval evidence about their product for the FDA to make a decision than they'd ever get from more trials in the US.

A "poster child" for the data acceptance and use restriction issues is the artificial cervical disc. Currently there are approximately fifteen (15) CE-marked artificial discs in successful use in Europe – including discs from ten (10) US manufacturers. (I don't have data for Asia or on the Americas, other than the US.)

Of those eight (8) US-invented discs, only three (3) are available in the US. Further, in the US, each of those three (3) has the restriction that only one disc may be implanted in any one patient – a decision successfully left to the product designer and patient expert, manufacturer and doctor, in the EU. This is critical as most spine patients need more than one disc.

Disc	CE date	# Levels	FDA	# Levels
Bryan	2000	C3 – C7; per dr. & manf.	2009	1 per FDA
ProDisc-C	2003	C3 – C7; per dr. & manf.	2007	1 per FDA
Prestige ST	2005	C3 – C7; per dr. & manf.	2007	1 per FDA
Cervicore	2008	C3 – C7; per dr. & manf.	In trials in 2008 @ 1 level	TBD
Kineflex	Pre-2005	C3 – C7; per dr. & manf.	In trials since 2005 @ 1 level	TBD
M6-C	2005	C3 – C7; per dr. & manf.	In trials since 2006 @ 1 level	TBD
Mobi-C	2006	C3 – C7; per dr. & manf.	In trials since 2006 @ 1 level	TBD
PCM	2003	C3 – C7; per dr. & manf.	Trials done 02/2010 @ 1 level	TBD
Prestige LP	2004	C3 – C7; per dr. & manf.	Unknown status	TBD
Secure-C	2003	C3 – C7; per dr. & manf.	In trials since 2006 @ 1 level	TBD

(Note: Data is based on research by the author.)

Despite having had to conduct the same types of trials and evidence gathering to earn the European CE-marking, each disc manufacturer has had to start from scratch when they decided to enter the US market. (See the chart above.) Are European bodies so different than US bodies that patient trials (the crux of approval processes) must be repeated?

Again, manufactures with a CE-mark are actually more prepared for FDA approval than those without. They bring with them both pre-approval evidence and post-approval data. For example, artificial cervical disc replacement surgery is conducted in the EU as commonly as fusion is conducted in the US; due to its long-term consequences, fusion is considered the procedure of last resort outside the US.

Going through more trials and more pivotal studies just because the data wasn't gathered in the US or isn't in the perfect format delays patient access for years and adds millions of dollars in manufacturer costs that will be

passed on to the patient, thus further affecting accessibility.

Regardless the current economic or political environment, the approval process needs to be more transparent and reliable to reduce cost and time to market, and to remove delays that are costing patients a fortune in quality of life, medications, medical expenses, and economic productivity. The US model isn't functioning as efficiently and effectively as other approval process models abroad. There must be change that serves patients.

A call to action

There are hundreds of thousands of US citizens waiting for access to thousands of medical devices that already have proven their mettle in trusted nations. Most of our fellow citizens don't have the resources or physical capability to get to devices that should be in common use in the US as they are already in other countries. I am asking you to help me to:

> *require the FDA to accept the regulatory findings of products with strong track records from other trusted countries and unions (i.e., from Europe, Australia, Japan, and others), and put them into the marketplace or, at a minimum, "fast track" them. Then monitor them as they currently do in the marketplace.*

The FDA CDRH approval processes are driving US inventors out and foreign inventors away from the US market. US patients go without or go overseas for medical technologies invented here.

The sooner we enact change, the sooner US patients will have access to the devices they need at a reasonable price – instead of waiting two (2) to ten (10) years for devices invented here and abroad.

Your fellow citizens desperately need your help. Many patients don't have time to wait.

Respectfully submitted,

Marti Conger

Marti Conger, M.Ed.
[redacted]

Mr. STEARNS. I thank the gentlelady.

Ms. Sagan, you are recognized for 5 minutes. I just urge everybody if possible to keep it to 5 minutes.

TESTIMONY OF PAM K. SAGAN

Ms. SAGAN. Chairman Stearns, Ranking Member DeGette and members of the committee, thank you for asking me to testify before you today.

My husband and I have three children, the youngest of whom, our daughter Piper, was diagnosed with type 1 diabetes at the age of 2 in 1989. She has lived over 20 years with this constant, frightening, deceptive and malicious disease.

I come before you today not only as a parent but as an advocate for tools and technology for my daughter and others with diabetes and with my enduring hope for a cure.

Piper has always been prone to hypoglycemic events—low blood sugar. They seem to come on hard and fast. I remember her almost drowning as a youngster after becoming unconscious from low blood sugar while taking a bath. College also brought one or two incidents a year where she slept into hypoglycemia and didn't wake up the next morning, requiring emergency medical care.

There is a chilling term that is the worry of every parent of a child with diabetes called "dead in bed." Kids are found dead in the morning after a completely normal evening the night before. Most of the time it is due to severe hypoglycemia. I don't want this to happen to my daughter or anyone else with diabetes, so you can understand where my fire comes from.

Just this past winter, Piper, now a 24-year old, had another severe hypoglycemic event. While working at a retail store, the last thing she remembers is closing the front door of the shop as she left to walk the 10 blocks to her apartment. My cell phone rang at home, and she slurred to me that she was locked out of her apartment. Upon further conversation, I realized that she was low. She had wandered her way home in a semiconscious state. She had crossed busy San Francisco city intersections at rush hour, she had fallen and scraped her hands as she walked, and she had lost bladder control. She finally ended up at her apartment, the keys were in her purse, but she didn't know what they were. She pulled out her cell phone and pushed the number one, my cell phone number. All this time, her continuous glucose monitor was alarming, but her blood sugar was too low to take action, and her insulin pump continued to pump insulin into her body, lowering her blood sugar even more.

This is life with type 1 diabetes. Type 1 diabetes occurs when the body's immune system attacks the cells in the pancreas that produce insulin. Insulin regulates glucose in one's body, and without it, a person with type 1 diabetes cannot live. There is no cure for this disease and it imposes an enormous physical, emotional and financial burden. On average, a child with diabetes will have to take over 50,000 insulin shots or infusions in a lifetime. Every hour of every day for the rest of her life, she will have to balance insulin, food and activity to try to prevent low and high blood sugars, and the devastating and costly complications: seizures, comas, kidney failure, heart disease, blindness and amputations. It

astounds me that diabetes costs our nation more than $174 billion a year and one in three Medicare dollars is spent to care for people with diabetes.

Because of these burdens, people with diabetes and their loved ones need timely access to innovative, life-saving technologies to help better manage the disease. Some breakthrough tools and technologies that protect against dangerous diabetes episodes are already available all over the world, but not available here in the United States.

I don't claim to be an expert on the regulatory process at the U.S. Food and Drug Administration, but as a parent with a daughter with diabetes, I am extremely frustrated that better technologies to help people with diabetes are delayed here in the United States. Low-glucose suspend systems have been approved for nearly 3 years and used safely in over 40 countries worldwide, but they are not available here in America. This technology is one critical example where our Nation is lagging behind in the approval of devices that would make living with this disease much safer. As background, these pumps stop delivering insulin automatically when a monitor indicates that the body's glucose levels are low. With this kind of pump, my daughter wouldn't receive more insulin when she is already low, causing her blood sugar to drop further and potentially causing a seizure, coma and even death. With the present FDA approval process, it will require a clinical trial conducted in this country, and a delay of years to conduct the study and compile the data before a decision is made. Kids are dying from hypoglycemia now. I want, and my daughter needs, this system available in the United States today.

In 2006, I was thrilled that the FDA recognized the importance of this technology and placed the artificial pancreas on its Critical Path Initiative. That was 5 years ago. With the funding from the Special Diabetes Program, for which I am so grateful to all the members of this committee for supporting, the artificial pancreas was tested favorably in a hospital setting. Now it is time to move to outpatient studies.

I implore Congress to continue to urge the FDA to move forward on next steps relating to low-glucose suspend systems and the artificial pancreas so that people with diabetes will remain healthier and safer until a cure is found, and I would lead the chorus of applause for the FDA when real progress happens, but it has to happen very soon. My daughter's life is depending on it.

[The prepared statement of Ms. Sagan follows:]

Testimony of Pam K. Sagan

Hearing Witness

Panel II

At the Hearing titled:

"FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs"

Wednesday, July 20, 2011, 10:30 a.m.

Before the

House Committee on Energy & Commerce

Subcommittee on Oversight and Investigations

2322 Rayburn House Office Building

Washington, D.C.

Chairman Stearns, Ranking Member DeGette and Members of the Committee: Thank you for asking me to testify before you today. My husband and I have three children; the youngest of whom, our daughter Piper, was diagnosed with type 1 diabetes at the age of two in 1989. She has lived over 20 years with this constant, frightening, deceptive and malicious disease. I come before you not only as a parent, but as an advocate for tools and technology for my daughter and others with diabetes, and with my enduring hope for a cure.

Piper has always been prone to hypoglycemic – low blood sugar – events. They seem to come on hard and fast. I remember her almost drowning as a youngster after becoming unconscious from low blood sugar while taking a bath. College also brought one or two incidents a year where she slept into hypoglycemia and didn't wake up the next morning, requiring emergency medical care. There is a chilling term that is the worry of every parent of a child with diabetes called "dead in bed". Kids are found dead in the morning after a completely normal evening the night before. Most of the time, it is due to severe hypoglycemia. I do not want this to happen to my daughter or anyone else with diabetes. So you can understand where my fire comes from.

Just this past winter, Piper, now a 24-year old, had another severe hypoglycemic incident. While working at a retail store, the last thing she remembers is closing the front door of the shop as she left to walk the 10 blocks to her apartment. My cell phone rang, and she slurred to me that she was locked out of her apartment. Upon further conversation, I realized that she was "low". She had wandered her way home in a semi-conscious state – she had crossed busy city intersections at rush hour, she had fallen and scraped her hands as she walked, and she had lost bladder control. She finally ended up at her apartment, the keys were in her purse, but she did not know what they were. She pulled out her cell phone and pushed the #1 – my cell phone number. All this time, her continuous glucose monitor was alarming, but her blood sugar was too low to take action, and her insulin pump continued to pump insulin into her body, lowering her blood sugar even more.

This is life with type 1 diabetes. Type 1 diabetes occurs when the body's immune system attacks the cells in the pancreas that produce insulin. Insulin regulates glucose in one's body and without it a person with type 1 diabetes cannot live. There is no cure for this disease and it imposes an enormous physical, emotional, and financial burden. On average, a child with diabetes will have to take over 50,000 insulin shots or infusions in a lifetime. Every hour of every day for the rest of her life she will have to balance insulin, food, and activity to try to prevent low and high blood sugars, and the devastating and costly complications: seizures, comas, kidney failure, heart disease, blindness, and amputations. It astounds me that diabetes costs our nation more than $174 billion a year and one in three Medicare dollars is spent to care for people with diabetes.

Because of these burdens, people with diabetes and their loved ones need timely access to innovative, life-saving technologies to help better manage the disease. Some breakthrough tools and technologies that protect against dangerous diabetes episodes are already available all over the world, but not available here in the United States.

I do not claim to be an expert on the regulatory process at the U.S. Food and Drug Administration, but as a parent with a daughter with diabetes, I am extremely frustrated that better technologies to help people with diabetes are delayed here in the United States.

Low glucose suspend systems have been approved for nearly three years and used safely in over 40 countries worldwide, but they are not available here in the U.S. This technology is one critical example where our nation is lagging behind in the approval of devices that would make living with this disease much safer.

As background, these pumps stop delivering insulin automatically when a monitor indicates that the body's glucose levels are low. With this kind of pump, my daughter wouldn't receive more insulin when she's already low, causing her blood sugar to drop further and potentially causing a seizure, coma, and even death. With the present FDA approval process, it will require a clinical trial conducted in this country, and a delay of years to conduct the study and compile the data before a decision is made. Kids are dying from hypoglycemia now. I want, and my daughter needs, this system available in the U.S. today.

Likewise, if the pattern continues, the next generation of these systems may be available in other countries years before they are available in America. The low glucose suspend technology is the first phase of an artificial pancreas, a combination of a continuous glucose monitor and an insulin pump with software that communicates between the two to automatically monitor glucose levels and administer insulin doses. Unlike the low glucose suspend pump, the artificial pancreas would address both high and low blood sugar levels.

In 2006, I was thrilled that the FDA recognized the importance of this technology and placed the artificial pancreas on its Critical Path Initiative. Since then, with funding from JDRF and the Special Diabetes Program, for which I am so grateful for this Committee's tremendous support, the artificial pancreas was tested favorably in a hospital setting. Now key trials are on hold until the FDA provides a roadmap for outpatient studies. Clinical experts provided a draft roadmap in March to help the process along. I am so grateful that a bipartisan majority of the House provided strong support for this effort with letters, led by Representatives DeGette and Whitfield in the House and several Members of this distinguished Committee, encouraging the FDA to move forward quickly to consider this proposal. The FDA announced recently that it will publish draft artificial pancreas guidance by December. It should not have to take this long. This technology could revolutionize diabetes care. It is imperative that the FDA provide reasonable guidance immediately, not later as we've seen with low glucose suspend systems.

I implore Congress to continue to urge the FDA to move forward urgently on next steps relating to low glucose suspend systems and the artificial pancreas, so that people with diabetes will remain healthier and safer until a cure is found. I want very badly to be an advocate for the work of FDA. And I would lead the chorus of applause for the FDA when real progress happens, but it has to happen very soon. My daughter's life is depending on it.

Thank you, Members of the Committee, for allowing me to testify on an issue so close to home. I am pleased to answer questions you may have.

Mr. STEARNS. Thank you.
Mr. Mandel, you are recognized for 5 minutes.

TESTIMONY OF MICHAEL MANDEL

Mr. MANDEL. Members of the subcommittee, thank you very much for the opportunity to testify on medical device regulation and its impact on health and innovation.

This statement draws heavily on a recent policy brief that I wrote for the Progressive Policy Institute where I am chief economic strategist. I am going to talk about one specific example where the FDA is apparently impeding innovation. I will then briefly discuss what we can do to boost innovation without hurting health and safety while expanding high-quality health care to underserved populations.

My major focus as an economist is the link between innovation and jobs. U.S. job growth has been weak since 2000. Surprisingly, innovation has been weak as well once we look beyond IT and communications. We got the iPhone but we didn't get gene therapy. We got Angry Birds but we didn't get enough health-improving, productivity-enhancing medical technologies. The question is why. There are plenty of culprits. Profit-seeking companies, inflexible doctors, out-of-control lawyers, myopic academics, the list could go on and on. But today I am going to focus on the FDA.

The FDA has a very tough and essential job: ensuring the health and safety of the American public. But over the years, people have regularly complained to me that the FDA imposes excessive requirements on the approval of new drugs and devices. No doubt the FDA has gotten stricter in recent years about requiring evidence of safety and effectiveness. However, by itself, that is not enough to show over-regulation. Health and safety is paramount, and no one wants dangerous drugs and devices put on the market. It could be that we were under-regulating before. However, in May 2011, I heard about one example that suggested over-regulation. This was MelaFind, a name that I had never heard before, a handheld computer vision device intended to help dermatologists decide which suspicious moles and spots should be biopsied for melanoma.

Not to go into detail here, but if MelaFind worked, it was easy to see how it could improve health and cut costs. Moreover, MelaFind could be used to augment care in low-income and rural areas. Equally important, the device was non-invasive. That meant it was as safe as possible, and it was an IT-driven expert system, which meant that it would get better over time as the computer power increased. Imagine my surprise when I discovered that the FDA staff had deemed MelaFind not approvable, and double my surprise when I read the briefing document that the FDA staff prepared for a panel of dermatologists, statisticians and other experts who were voting on whether to recommend MelaFind for approval. The FDA briefing document started with a very reasonable analysis of the shortcomings of the MelaFind test results. I was initially quite sympathetic to FDA's perspective but when the FDA started listing its broader objection to MelaFind and what it expected the device to do, it quickly became clear that the agency was using a set of standards that no first-generation device could ever reach.

Just a couple of striking ones. The FDA objected because the study did not find "a clinically significant difference between MelaFind and the examining dermatologist." The agency also objected because the device was not demonstrated to make inexperienced doctors the equal of experienced dermatologists. Let me repeat that. The FDA apparently was saying that in order to be approved, that MelaFind had to beat experienced dermatologists and had to turn inexperienced doctors into the equivalent of board-certified dermatologists. These are great goals. These are fantastic goals. However, they are also goals that no first-generation device can ever reach. Failing to approve MelaFind is the equivalent of rejecting the first cell phone on the grounds that callers might mishear important emergency messages. Or think about a government body telling Steve Jobs in 1977 that the first Apple computer was not approvable because he had not submitted a study showing Apple users could be trained to produce the same results as users of mainframe computers.

Because MelaFind is non-invasive, it gives us a clear window into the FDA's approach that we don't get from other devices and drugs that may have negative side effects. As an economist, it worries me that we are missing health-improving, productivity-enhancing devices and drugs because the FDA has too narrow a perspective. Thank you.

[The prepared statement of Mr. Mandel follows:]

STATEMENT OF MICHAEL MANDEL, PHD

CHIEF ECONOMIC STRATEGIST
PROGRESSIVE POLICY INSTITUTE

U.S. House Committee on Energy and Commerce

Subcommittee on Oversight and Investigations

July 20, 2011

SUMMARY

As the key gatekeeper for pharmaceutical and device innovation, the Food and Drug Administration (FDA) has a tough job. If it is too lenient, it will allow the sale of drugs and medical technology that could harm vulnerable Americans. Too tight, and the U.S. is being deprived of key innovations that could cut costs, increase health, and create jobs.

This statement draws extensively on a recent policy brief that I wrote for the Progressive Policy Institute, where I am Chief Economic Strategist. In this statement, I address the question: Is the FDA unintentionally choking off cost-saving medical innovation? First, I discuss the difficulty of assessing whether the FDA is under-regulating or over- regulating new drugs and devices, given the desire for safety. I then show how the FDA is clearly applying "too-high" standards in the case of one noninvasive device currently under consideration—MelaFind, a handheld computer vision system intended to help dermatologists decide which suspicious skin lesions should be biopsied for potential melanoma, a life- threatening skin cancer. I then draw analogies to development of the early cell phones and personal computers.

STATEMENT

Mr. Chairman, Ranking Member DeGette, members of the subcommittee. Thank you very much for the opportunity to speak on medical device regulation, and its impact on health, innovation, and jobs.

This statement draws heavily on a recent policy brief that I wrote for the Progressive Policy Institute, where I am currently Chief Economic Strategist. ("How the FDA Impedes Innovation: A Case Study in Overregulation", June 2011). I am also affiliated with the Mack Center for Technological Innovation at Wharton at the University of Pennsylvania, as a senior fellow. Until 2009, I served as Chief Economist at BusinessWeek, where I helped direct the magazine's domestic and international economic coverage. I've written three books on uncertainty, innovation and growth, and one basic economics textbook.

My major focus as an economist is the link between innovation and jobs. We all know that U.S. private sector job growth has been weak for the past decade. Surprisingly, innovation has been weak as well, once we get beyond the IT/communications sector. In a piece I published in 2009, I constructed a list of potential innovations that were receiving major investments from venture capitalists and corporations in 1998. I then showed that the commercial impact of most of them were far less than expected ten years later, outside of the IT/communications sector. So we got the iPhone, but we didn't get gene therapy.

INNOVATION IN MEDICINE

If we look back at the economic history of the past 200 years, one pattern stands out clearly—new technologies start out expensive, but then end up cutting costs over time. For example, gasoline-driven tractors were initially much costlier and less reliable than horses. Over time, however, tractors were improved and made much less expensive, and the resulting shift to mechanized agriculture helped drive down the cost of producing food.

Similarly, when cell phones were first introduced in the 1980s, they were bulky, heavy devices which retailed for $4000, provided terrible reception and could barely fit in a briefcase, much less a pocket. After 20 years of evolution, iPhones and Android smartphones are slender, light, relatively cheap and far more capable than their ancestors.

One unfortunate exception to this historical pattern is healthcare. The United States devotes roughly one-third of its R&D spending, public and private, to the biosciences, so presumably we should be getting plenty of useful innovation.[1] Yet the cost of healthcare per person keeps rising, faster than the aging of the population would account for. As a result, the conventional wisdom is that healthcare technology, rather than holding down costs, has actually increased them.

This breakdown of historical precedent has generated plenty of finger pointing. In no particular order, drug companies have been blamed for focusing too much on profit rather than on cost-saving advances; lawyers have been blamed for frivolous malpractice suits that have doctors practicing defensive medicine; physicians have been blamed for being too inflexible and focused on their own income; politicians have been blamed for setting up an entitlement system that encourages excess spending; and the government's main health research funding agency,

NIH, has been blamed for overemphasizing academic research rather than product development

FDA AND REGULATION

For the purposes of this hearing, however, I will focus on the FDA, which has been criticized for imposing excessive requirements on the approval of new drugs and medical devices. Three facts are clear. First, the FDA's regulatory reach and intensity has increased over the past 10 years. FDA employment grew by 33 percent between 2000 and 2011, even as employment in the regulated industries—pharmaceuticals, medical devices, and biotech--only rose by 3 percent.

Second, in the wake of high-profile episodes such as the Vioxx case, the FDA has gotten stricter about requiring evidence of safety and effectiveness before approving new drugs. Third, the number of new drugs approved fell sharply over the past decade compared to the decade before.

Still, these three facts alone are not enough to show that the FDA is over-regulating today. Many would argue that the changes were necessary, because the FDA was under-regulating previously. Indeed, few people would want the FDA to approve drugs or devices that carry potential safety risks for patients.

AN EXAMPLE OF OVERREGULATION

However, there is one ongoing example that suggests the FDA might have crossed the line into over-regulating and suppressing innovation. This is the case of MelaFind, which as noted above, is a handheld computer vision device intended to help dermatologists decide which suspicious

skin lesions should be biopsied for potential melanoma. The device is pointed at a lesion, the visual image is rapidly compared to a computerized database, and the results are reported to the doctor.

A device such as MelaFind, if approved, could be a very useful tool, since melanoma is easy and cheap to treat when caught early, and expensive and difficult to treat if detection is delayed. MelaFind would provide an immediate second opinion for dermatologists, and a dermatologist working long hours in an inner city or rural clinic could use MelaFind's expert system to provide consistent advice. This availability of this tool is especially important as cost pressures force doctors to spend less time with each patient.

In order to get approval, Mela Sciences, the company that created MelaFind, did a multi-year study of the accuracy of the device compared to a panel of dermatologists. The company claims that it passed the test that the FDA had agreed to.[2] Indeed, on some dimensions of the study the device did better than the panel of dermatologists.

Nevertheless, the FDA staff deemed the device "not approvable," saying that MelaFind "puts the health of the public at risk."[3] Despite the strong negative response from the FDA, the company requested that the device be assessed by a panel of dermatologists, statisticians, and other medical experts. The advisory panel met in November 2010 and voted narrowly to recommend approving MelaFind.[4] Nevertheless, the FDA has not yet approved the device.

To understand why this is an example of overregulation, let's look at some of the medical background. The early detection process for melanoma has two steps: First, the dermatologist or

other skilled physician checks the patient to identify potentially suspicious skin lesions. Second, the doctor decides which lesions to biopsy—remove in part or whole--and send to a lab to be checked for cancer.

There are two important points here: First, it's not feasible or desirable to biopsy all skin lesions. Biopsies are expensive and potentially disfiguring, depending on the location and the type of tool used. The goal, medically and financially, is to biopsy the fewest number of lesions consistent with catching the maximum number of melanomas.

Second, identifying which lesions to biopsy is more of an art than a science. Put five dermatologists in a room with a patient, and each of them might pick a somewhat different set of lesions to biopsy. And, of course, the chance of errors goes up when dermatologists with less experience or training are doing the screening.

Ideally, dermatologists could use a second opinion—another set of eyeballs--to help make a decision about which suspicious lesions to biopsy. That's the role of MelaFind, which is a combination of computer vision linked to an expert system. The handheld device effectively takes a picture of the lesion, compares it to an internal database, and then indicates whether the lesion should be biopsied.

THE FDA'S RATIONALE

There are two important points about MelaFind relevant to the topic of this paper. First, it is noninvasive. As a computer vision system, MelaFind stands at the low end of the spectrum of possible safety risks—less risky to patients than most drugs, implanted devices such as stents,

pacemakers, and joint replacements, and devices that emit penetrating radiation.

Second, as an expert information technology system, the company has a clear path to improving the performance of the device over time, just like virtually every information technology device has improved its performance over time.

So why then did the FDA come out so strongly against MelaFind? In the briefing document for the November 2010 panel meeting, the agency made several arguments:[5]

- The device did not do better than the experienced dermatologists in the study ("the FDA review team does not believe this is a clinically significant difference between MelaFind and the examining dermatologist")
- The device was tested on lesions identified by experienced dermatologists, not on the broader set of lesions that might be identified by "physicians less experienced than these dermatologists."
- The device did not find every melanoma in the sample ("Since the device is not 100% sensitive, if use based on the device's diagnostic performance reduces the number of biopsies taken, harm could ensue in the form of missed melanomas.")
- The device was not demonstrated to make inexperienced physicians the equal of experienced dermatologists ("Currently, formal training is offered to physicians to become board certified dermatologist and thus be able to diagnose clinically atypical lesions. The FDA review team would have to compare this board certification training to that offered by the sponsor to those physicians operating MelaFind to determine if it is found adequate.")

To summarize, the FDA seems to be saying that it cannot approve MelaFind unless the device can:

- Outperform experienced dermatologists
- Perform well on any lesion that an inexperienced doctor might find suspicious
- Never miss any melanomas
- Turn an inexperienced doctor into the equivalent of a board-certified dermatologist.

This is a standard that no first-generation device can ever reach. **If the FDA fails to approve MelaFind, it would be the equivalent of rejecting the first cell phone on the grounds that callers might mishear important messages.**

RESETTING THE STANDARD

By not approving MelaFind, the FDA is clearly blocking innovation. The device is far from perfect, but it's a real-time system that by some measures does as well as an experienced dermatologist in identifying lesions to be biopsied.

What's more, the philosophy of the device is clearly pointing in the right direction—the use of information technology to improve medical decision making and treatment, with the ultimate long-term goal of both improving health and lowering costs.

But beyond the approval or rejection of one particular device, the larger issue is whether the U.S. has unintentionally set up a system of approvals that are biased against cost-saving "disruptive innovation." A disruptive innovation, as identified by Clayton Christensen, starts out as less capable

than existing technologies, but as the innovation evolves, it gets both cheaper and more powerful. The first automobiles, for example, were both more expensive and less reliable than a horse. Similarly, the first personal computers were basically toys compared to the existing minicomputers and mainframes. But they got better and cheaper over time.

From that perspective, it's clear that a government regulatory body with "too-high standards" can have the effect of choking off innovation. Imagine how the history of computing would have been different if Steve Jobs and Steve Wozniak had to prove that the Apple I could meet government performances standards before it could be sold.

With fairly modest changes, FDA standards can be adjusted to encourage cost-saving innovation without compromising safety. That's essential for growth and jobs going forward.

---

1 "Where the U.S. is Building Knowledge Capital," Innovation and Growth blog, December 21, 2010.

2 More precisely, the company claims that it has a 'binding protocol agreement' that the FDA has violated. (See an explanation here). This is an exceptionally important point, but not germane to this paper.

3 *FDA PMA P090012 Executive Summary*, MELA Sciences, Inc., MelaFind, November 18, 2010.

4 "Mela Shares Surge After FDA Panel Vote," Wall Street Journal (online), November 19, 2010.

5 *FDA PMA P090012 Executive Summary*, November 18, 2010.

Mr. STEARNS. Thank you.
Dr. Ianchulev, you are recognized for 5 minutes.

TESTIMONY OF SEAN IANCHULEV

Mr. IANCHULEV. Thank you. Mr. Chairman, Ranking Member DeGette and members of the subcommittee, I am Dr. Ianchulev, and I would like to thank you for the opportunity to share my personal experience with the FDA and the regulatory process and its impact on patient care, innovation and development of new technologies in this country. These are my own opinions, and I share them to you from the perspective of a physician, innovator and developer of some new therapeutics and devices.

In the way of background, I am a physician, eye surgeon who uses medical devices and technology to treat and prevent blindness. I am an associate clinical professor on the faculty of UCSF School of Medicine, where I see firsthand the translation of research into patient care, and as the developer and inventor of new technologies in the field, I have led innovative treatments through the regulatory process with the FDA and I have direct experience with the drug and device side of the FDA in addition to experience with the European regulatory authorities.

Physicians such as myself feel privileged to be educated, practice and advance medicine in the United States. The United States has been a leader in cutting-edge innovation traditionally, and my field, ophthalmology, is a bright example to that effect. In fact, the most common device implanted today is the intraocular lens implant for cataracts, and this has been one of the most successful, effective and safe treatments to date based on innovation of the 1980s and 1990s and based on leadership of the FDA at that time with a streamlined regulatory process.

Today more than ever, we need best-in-class technology in service to our aging population and it is unfortunate that patients are starting to seek care from foreign doctors who are now trained and have hands-on experience with technologies we see much later in the United States, as we heard today. As a physician who not only delivers the standard of care but also innovates in my field, I have failed a number of times to treat patients with what I think is the best treatment for them. In fact, I see more and more patients seeking the often-challenging offshore route in search of interventions that are not available here with much added cost, frustration and pain. When recently asked by a patient suffering from a degenerative, blinding eye disease about a therapy not approved in the United States but available in other countries, I had to stay silent. The patient ended up traveling to Canada to receive treatment for which he paid out of pocket.

But I would like to go beyond the anecdotal experience and ask the bigger question: what innovative first-class therapies are we delivering to patients today? Let us take the field of ophthalmology, which is a good example with its high degree of technical innovation and device utilization. To check the innovation pulse prior to this hearing on the way here, I reviewed all of the FDA-approved PMA devices in my field over the past 5 years. As you aware, the PMA class III devices is the lifeblood of innovation and some of the most advanced, complex devices for life-sustaining or, in my case,

vision-sustaining, treatments are approved through this process. I reviewed the labels of all 12 such devices I could find on the FDA Web site. At the time of approval, all of them had been approved not only in the EU but in many as 20 to 40 countries before they were approved in the United States. In addition, some of the devices already had vast clinical experience dwarfing the FDA clinical trial numbers and in some examples those were more than 100,000 patients treated worldwide before FDA approval. In one illustrative case with the cumulative world experience of more than 60,000 patients, the FDA label spoke only of 300 patients in the registration trials, too few and too late.

Avoiding a long discourse on the meaning of the symptomatic state, it is not hard to see that we have failed to deliver best-in-class innovation. More importantly, we now see that new technologies are not only perfected abroad but are developed and commercialized to their full extent and companies now execute not only on small feasibility studies but implement their main validation studies, their clinical research programs and even product launches abroad, as evidenced by a recent MDVC report. What follows with that is the departure of talent, expertise and patients.

The FDA is the gateway for new therapies, and as a vigilant gatekeeper, the regulatory process has to ensure safety and efficacy, but it has to facilitate innovation, and examples of that are right in the halls of the FDA. As a drug developer who headed the clinical research and development programs at one of the most successful approved biologic therapies for eye disease, Lucentis for macular degeneration, I have added comparative experience from the CDER, whose input and oversight were critical in the execution of this highly complex, rigorous therapeutic program of biologics and resulted in the commercialization of a groundbreaking therapeutic which helps hundreds of thousands of patients today.

So this program was not only successful but exemplary in many ways of how the regulatory process should work and was referenced by the FDA itself in a published guidance to industry for best-in-class drug development. The key learnings from this experience—explicit guidance to companies and investigators, consistency and transparency of feedback in the review process, and a high level of in-house expertise from the FDA reviewers.

My experience with the development of new technologies is that the pathway to innovation is challenging and it is necessary to take calculated risks in a thoughtful and deliberate way and to protect patients. We need safe and effective treatment for all patients and it is critical that we have the best-in-class regulatory process to do justice to the high level of passion, hope, talent and resources this country invests in the innovation process in helping patients. Thank you.

[The prepared statement of Mr. Ianchulev follows:]

July 20, 2011

Congressional Hearing on the Impact of Medical Device Regulation on Jobs and Patients

Testimony Sean Ianchulev, MD MPH

Mr. Chairman, Ranking Member DeGette and Members of the Subcommittee, I am Dr. Sean Ianchulev, and I would like to thank you for the opportunity to share my experience with the FDA and the regulatory process and its impact on patient care, innovation and the development of new technologies. The opinions I share are solely mine and not of the entities I am associated with and they reflect my experience as a physician, innovator and developer of new therapeutics and devices.

I will support the following statement with additional information.
I believe we have an overly burdensome CDRH regulatory process which negatively impacts all stakeholders in the medical device field - innovators, physicians, patients and investors. It probably negatively impacts the agency itself which devotes enormous diligence to maintain integrity, expertise and vigilance – all good causes which deserve better return on the effort invested. Much value can be obtained from process improvements that would increase efficiency, transparency, communication and streamline the regulatory process to achieve operational excellence and meet the needs of the new decade.

As a clinician and eye surgeon, I use medical devices and therapeutic intervention to treat serious medical problems and prevent blinding conditions such as glaucoma, cataract and macular degeneration. In fact, the most frequently implanted medical device (more than 3 million implantations per year) is the intraocular lens implant for cataract surgery - a product of groundbreaking innovation which transformed clinical care and patient wellbeing and is considered one of the best examples of a safe and effective clinical intervention today.

As an innovator I have considerable experience with both divisions of the FDA - the CDER and CDRH. As a drug developer who headed the clinical research and development of one of the most successful approved biologic therapies for eye disease (Lucentis ® for macular degeneration) I have the added comparative experience with the CDER whose input and oversight were critical in the execution on this highly complex, rigorous therapeutic program and resulted in the commercialization of a groundbreaking therapeutic with more than $2Bn annual sales and great impact for patients, physicians, industry and jobs. Simultaneously, as a physician executive and chief medical officer for a medical device company which has raised more than $50 million to finance the development of an eye implant - a Class III device and one of the few medical devices in an ongoing PMA process, I have direct experience with the

CDRH in today's environment which gives me a perspective into some of the manifest challenges at the division.

Lastly, as a health care professional who is licensed both in the US and the EU and who frequently participates in clinical, academic and professional exchanges/collaborations in Europe, and spends significant amount of time with fellow European clinicians, I am acutely aware of parallels and contrasts in the changing paradigms of clinical practice and access to new technology across the Atlantic.

Physicians such as myself feel privileged to be educated, to practice and advance medicine in the US where access to cutting-edge innovation and latest technology has been the marquee of American health care. Medical devices represent a significant part of this innovation particularly for a surgeon like myself and in a field such as ophthalmology which boasts a high level of device innovation. As a leader in the medical device field over the past several decades, the US has been able to deliver enormous benefits to patients while cultivating an environment of innovation and expertise with simultaneous economic benefit in terms of highly qualified jobs. In my field, there are many examples but most salient is the fact that we can now successfully treat cataracts (one of the few chronic degenerative diseases to be cured) with a safe and effective implant technology which was developed mainly in the US in the 1980s and 1990s and perfected more recently.

Since regulatory approval is the gateway for allowing physicians to use pioneering technologies, there is no doubt in my mind that the US regulatory leadership in the past with a streamlined and responsive best-in-class regulatory process was in part responsible for these advances as it encouraged innovators, physicians and industry to deliver new safe and effective therapies. Similarly, there is no doubt that if we lack the necessary leadership and regulatory innovation today, it will be particularly detrimental in a global world where knowledge and expertise have no boundaries.

Since 2007, the review process for devices appears to have changed with a momentous swing towards a state of hyper-vigilance and conservatism which has significantly increased the burden, cost and timelines for the introduction of new devices. The sharp decline in the productivity of the regulatory pipeline (with a decrease in PMA filings- only 15 in 2009) is concerning at this very juncture when few diseases have been cured and there is great unmet need for new and better therapies to address the aging population.

Today, the overburdened regulatory process poses several dilemmas with real impact on all stakeholders, including the FDA.

The Patient Dilemma:
The direct patient experience is always the best indicator for whether we fail in our job in the health care field. As an eye surgeon I treat patients who are losing their sight either due to advancing cataracts or glaucoma or macular degeneration. As a physician who

not only delivers the standard of care, but also innovates in the ophthalmic field, I have failed on a number of times to treat patients with what I would have thought is the best therapeutic approach. On several occasions, I have had to refer patients to other countries (Europe and Canada) to receive the necessary treatment because the medical devices were not available in the US and were years away from being commercialized. I appreciate the counterpoint on fully characterized product efficacy and safety for FDA approval, but the already available worldwide clinical experience from colleagues and the peer-review literature well ahead of FDA registration in the US can inform physician clinical judgment and allow educated patient decision on the best therapeutic approach. In reality, even with approved FDA treatments, the product label rarely predicts the individual patient response and clinical experience.

In the ophthalmic field, virtually most technologies that were PMA approved in the US in the last 5 years, as well as many new technologies currently captive in a convoluted approval process (such as new Intraocular lenses, minimally invasive glaucoma stents, other intraocular implants), have been available in the rest of the world for many years, allowing foreign clinicians to practice advanced medicine and participate in new improvements and future innovation. In the US, the slow approval process limits physician access to such technologies even if there is ample data and experience from abroad. This leads to another dilemma: FDA or physician control on prescribed treatment choice at the point of care. Replacing physician judgment, experience and decision-making with a product label is not a good idea and seems to represent a dangerous trend in the more recent regulatory philosophy and process in the US today. While Congress never gave the FDA a mandate to regulate physician practice, such is being effectively exercised by curtailing access to new technology and products. Obviously, the balance between prescriptive labeling and physicians' access and judgment on how to use these new technologies is very different in the US and other developed countries, such as EU, Japan and others.

The Innovation Dilemma:
The ophthalmic field could be a good example as it is one with traditionally high level of technological innovation with a multitude of surgical and diagnostic instruments such as intraocular implants and lasers. However, due to the systematic problems of increased cost and hurdles of the regulatory process, there are multiple classes of innovative technologies that are languishing in a state of uncertainty or prolonged validation. These include new and potentially superior intraocular lens implants for cataracts, stent technologies for minimally invasive treatment of glaucoma and iris reconstruction implants and others such as cross-linking technologies. These are not single products but often classes of products and multiple companies affected.

In my opinion, we should be doing a better job of cultivating these innovative approaches in a much more hospitable and expedient regulatory environment. In fact, most of these technologies are registered and available products in the European countries under the CE mark.

Avoiding a long discourse on the meaning of this symptomatic state, it is not hard to see that we have failed to deliver new and innovative device technology to patients and clinicians in the US.

The Developer's Dilemma:
One of the most palpable dilemmas that comes up among medical technology developers is the 510K vs. the IDE PMA pathway. The IDE PMA process for Class III devices has been the most affected with the highest degree of regulatory uncertainty and slow-down. This has alienated innovation in this important category which is evidenced by the very few PMAs granted more recently (only 15 in 2009). This is most concerning because the PMA is the "lifeblood" of true innovation and pioneering in medical devices - some of the most significant advances derive from the IDE/PMA process such as cardiovascular stents and other implants. The process of securing unconditional approval and initiation of an IDE in this class of devices has become so burdensome that I am aware of timelines exceeding a year and a half before the sponsor can secure full unconditional approval - that is just to start the study enrollment. *As someone who has worked with the CDER drug division on a complex biologic program before, this makes a device IDE a hard proposition even for a well funded biopharma.* In fact, a fresh example from the ophthalmic device field, where it is much easier to approve a drug for the treatment of glaucoma with primary efficacy endpoints between 3 to 6 months only, versus a minimally invasive stent with CDRH requirements of 12 months for the primary efficacy endpoint. In fact, I stand corrected - within the last year, the CDRH requirements for the primary efficacy endpoint in this indication increased further from 12 to 24 months without clear transparency, advanced notice, stated rationale or guidance documents.

Another developer's dilemma facing device innovation is operating in the US vs. the rest of world. Several reports provide informative data and statistics on this, and in my experience, there is an increasing trend where companies not only do early clinical feasibility testing abroad, but initiate their main validation studies, their registration programs and more recently their primary commercial activities. And since US doctors will not have experience with these technologies, it may not be long before patient care and referrals follow the offshore route. This does not mean to advocate that the European CE mark process is perfect for implementation here, but if the F*DA were to do a robust randomized comparative trial/assessment between the European and US registration systems, the regulatory performance outcomes may not only be statistically significant but clinically and socially meaningful.* And there are examples (probably not just a few outliers) where the delay in approval timelines between CE mark and PMA exceeds half a decade.

The Academic Dilemma:
As a physician who is also a clinical faculty and teaches resident clinicians, in my professional path, I have been associated with two leading medical research

institutions- Harvard Medical School, Boston, MA and UCSF, San Francisco, CA. Research and innovation is critical to their missions. The only way to innovate is to move technology from the labs to patients, and the vehicle for this is industry, enabled by the technology transfer process. A bottleneck in the regulatory process will invariably affect our ability to conceive and initiate technological innovation in academia, hurting education, universities and researchers.

In summary, my experience is consistent with some of the recent data suggesting an overburdened regulatory process which impacts negatively on all stakeholders in the medical technology field - patients, physicians, innovators and investors. Significant improvement can be realized by increasing efficiency, transparency, communication and streamlining the regulatory process to meet the needs of the new decade.

Mr. STEARNS. Thank you.
Dr. Curfman, you are recognized for 5 minutes.

TESTIMONY OF GREGORY D. CURFMAN

Mr. CURFMAN. Thank you, Chairman Stearns, Ranking Member DeGette and other distinguished members of the subcommittee. My name is Gregory Curfman. I am a cardiologist and I am the Executive Editor of the New England Journal of Medicine.

For nearly 200 years, the New England Journal of Medicine has been publishing research articles on new drugs and medical devices. We are strongly committed to innovation. Vigorous innovation in medical products is critical to the health of our Nation. But we have learned that innovation in medical treatments does not come easily. While some new drugs and devices succeed, others unfortunately fail, in many cases, owing to serious problems with safety. Innovation is essential to the future of our Nation but innovative medical products cannot succeed unless they are both effective and safe. Sensible quality assurance does not stifle innovation, it promotes it and avoids costly nightmare scenarios caused by flawed and potentially dangerous medical devices.

Let me give two recent examples of innovative medical devices, one from the field of cardiology and the other from the field of orthopedic surgery, both of which were approved by the FDA by the 510(k) fast-track process, but which were later found to be seriously defective even while they were being implanted in many thousands of patients.

The first example, from the field of cardiology, is the Sprint Fidelis implantable cardioverter-defibrillator lead, which was manufactured by Medtronic. This lead, which delivered an electric shock to the heart in order to halt potentially fatal heart rhythms, was approved by the FDA by the 510(k) process without clinical testing. The defibrillator lead received considerable hype as a major innovation in defibrillator technology. However, soon after fast-track approval of the Sprint Fidelis, it became clear that the lead was prone to fracture, which resulted in inappropriate shocks in many patients and caused at least 13 deaths. The lead was eventually withdrawn, but only after it had been implanted in over a quarter of a million patients worldwide. Thus, inadequate premarket testing and a fast track to FDA approval, resulted in a devastating situation for patients.

The second example, from the field of orthopedic surgery, and Congressman Waxman referred to this earlier, is a type of artificial hip implant known as the metal-on-metal design. Hip implants originally consisted of a metal ball inserted into a plastic cup. In newer models, which were widely hyped as a major technological innovation, the plastic was replaced with a metal alloy, the so-called metal-on-metal design. The new design was approved by the 510(k) fast-track process and did not undergo clinical testing, only bench testing. Not long after FDA approval, reports of shedding of metallic debris and failure of the metal-on-metal implants began to surface, and upwards of tens of thousands of patients have thus far been adversely affected.

Unfortunately, bench testing of the device did not faithfully reproduce the wear and tear of real life. Thus, an apparently minor

alteration in design—replacement of plastic with a metal alloy—resulted in nothing short of a public health nightmare.

These are sophisticated engineering devices that we are talking about. These two examples vividly demonstrate that the glamour of innovation does not always work out well for patients. Innovation in medical devices must go hand in hand with a careful assessment their efficacy and safety. Such quality control measures do not imperil innovation; they advance it, they secure it.

As for the European Union, the timelines to device approval there are only modestly shorter than in the United States, and it is of concern that in Europe, in contrast to the United States, the highest risk-devices, so-called class III devices, do not have to be shown to improve clinical outcomes prior to their approval. That is something to think about.

Mr. Chairman, innovation in medical devices is a high priority for our Nation, but to be truly innovative and to avoid costly mistakes, there must be solid evidence that new medical devices are both effective and safe. Thank you, Mr. Chairman.

[The prepared statement of Mr. Curfman follows:]

The NEW ENGLAND JOURNAL of MEDICINE

TESTIMONY OF GREGORY D. CURFMAN, M.D.
EXECUTIVE EDITOR
NEW ENGLAND JOURNAL OF MEDICINE
BOSTON, MASSACHUSETTS

HEARING:
REGULATORY REFORM SERIES #5
FDA MEDICAL DEVICE REGULATIONS:
IMPACT ON AMERICAN PATIENTS AND JOBS

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
HOUSE COMMITTEE ON ENERGY AND COMMERCE

WEDNESDAY, JULY 20, 2011

Chairman Stearns, Ranking Member DeGette, and other distinguished members of the Subcommittee on Oversight and Investigations, I want to thank you for inviting me to participate in this important hearing. My name is Gregory Curfman, and I am a cardiologist and the executive editor of the *New England Journal of Medicine*.

For nearly 200 years, the *New England journal of Medicine* has been publishing research articles on new drugs and medical devices. Our publication is strongly committed to innovation in medical therapies. Vigorous innovation in medical products is critical to the health of our Nation, but we have learned that innovation in medical treatments does not come easily. While some new drugs and devices succeed, others unfortunately fail, in many cases owing to serious problems with safety. Much of our work at the *New England Journal of Medicine* is focused on ensuring that the efficacy, safety, and potential hazards of medical products are transparently presented in the articles we publish.

Innovation is essential to the future of our Nation's health, but innovative medical products cannot succeed unless they are both effective and safe. Proper procedures must be in place to ensure both the safety and effectiveness of new medical products before they are brought to market. Sensible quality assurance does not stifle innovation; it promotes it and avoids costly nightmare scenarios caused by flawed and potentially dangerous medical devices.

Patient safety is a national concern. Major stakeholders throughout our health care system agree that every step must be taken to ensure that medical interventions, used with the intention of improving patients' health, are as safe as possible. But every medical intervention has benefits and risks. Patient safety can be ensured only when novel drugs and devices are rigorously evaluated in regard to their efficacy and safety. As the Institute of Medicine has made clear,

medical devices and drugs need to be assessed for risks and benefits not just prior to marketing, but throughout their life cycles. (1)

Let me give two recent examples of innovative medical devices, one from the field of cardiology and the other from the field of orthopedic surgery, both of which were approved by the FDA by the 510(k) fast-track process, but which were later found to be defective even while they were being implanted in many thousands of patients.

The first example, from the field of cardiology, is the Sprint Fidelis implantable cardioverter-defibrillator lead, which was manufactured by Medtronic. This lead, which delivered an electric shock to the heart in order to halt potentially fatal heart rhythms, was approved by the FDA by the 510(k) process without clinical testing. The defibrillator lead received considerable hype as a major innovation in defibrillator technology. The company made the case that it was substantially equivalent to an existing lead that had undergone clinical safety testing and had been on the market for some time. The company also claimed that only minor modifications had been made to the original lead. However, soon after fast-track approval of the Sprint Fidelis, it became clear that the lead was prone to fracture, which resulted in inappropriate shocks in many patients and caused at least 13 deaths. The lead was eventually withdrawn in 2007, but only after it had been on the market for 3 years and had been implanted in over a quarter of a million patients worldwide. Thus, inadequate premarket testing and a fast track to FDA approval, in which corners were inappropriately cut, resulted in a devastating situation for patients.

It is also noteworthy that because of the U.S. Supreme Court's ruling in an important federal preemption case, *Riegel v. Medtronic* (2), the manufacturer could not be sued under state law by patients alleging harm from the Sprint Fidelis lead. Since the Supreme Court ruling in *Riegel*, thousands of lawsuits against medical-device manufacturers

have been tossed out of court by judges following the Court's decision in deeming such lawsuits to be preempted. (3) Such preemption, which removes any legal recourse for injured patients, defies logic in that it applies only to medical devices, not to drugs.

The second example, from the field of orthopedic surgery, is a type of artificial hip implant known as the metal-on-metal hip. Hip implants originally consisted of a metal ball inserted into a plastic cup. In newer models, which were widely hyped as a major technological innovation, the plastic was replaced with a metal alloy (the so-called "metal-on-metal" design). The new design, which, like the Sprint Fidelis lead was approved by the 510(k) fast-track process, did not undergo clinical testing, only bench testing. Not long after FDA approval, reports of and shedding of metallic debris and failure of the metal-on-metal implants began to surface, and upwards of tens of thousands of patients have thus far been adversely affected. Unfortunately, the bench testing of the device did not faithfully reproduce the wear-and-tear of real life. Thus, an apparently "minor" alteration in design – replacement of plastic with a metal alloy – resulted in nothing short of a public health nightmare.

These two examples vividly demonstrate that the glamor of innovation does not always work out well for patients. Innovation in medical devices must go hand-in-hand with a careful assessment their efficacy and safety. Such quality-control measures do not imperil innovation, they advance it.

In preparing this testimony, Mr. Chairman, I reviewed two recent reports on medical technology innovation and regulation, the first written by Joshua Makower and Aabed Meer (4), and the second issued by the California Healthcare Institute (5), a policy research and advocacy organization. As a medical journal editor, I conducted careful reviews of these reports and concluded that both are promotional pieces for the medical device industry and do not

represent rigorous research. Because of serious flaws in how these reports were generated, they could not survive peer review procedures at serious medical journals and would not be publishable in peer-reviewed publications.

Finally, Mr. Chairman, I would like to make a comment about the regulation of medical devices in the European Union, an issue that was discussed in both reports (4, 5). It was argued that because regulatory procedures are simpler (i.e., less rigorous) in the EU than in the US, devices get to market and to patients faster. In fact, the time lines to approval are only modestly shorter in the EU, and it is worrisome that in Europe the highest-risk devices (so-called class III devices) do not have to be shown to favorably affect clinical outcomes prior to approval (6). In contrast, when class III devices undergo premarket approval (PMA) in the US, there must be an evidence base showing not only that the device performs as it is supposed to, but also that it favorably affects clinical outcomes.

Mr. Chairman, I conclude by underscoring the high priority of innovation in medical devices to our Nation, but to be truly innovative medical devices must be shown to be effective and safe. Cutting corners in quality control will inevitably result in costly medical nightmares down the road.

Thank you, Mr. Chairman, for your attention.

1. Challenges for the FDA: the future of drug safety – workshop summary. Washington, DC: National Academies Press, 2007.
2. Riegel v. Medtronic, 552 U.S. 2 (2008).
3. Kyle RH. In re Medtronic, Inc. Sprint Fidelis lead products liability litigation. Multidistrict litigation no. 08-1905 (RHK/JSM). Memorandum opinion and order. U.S. District Court of Minnesota. January 5, 2009. (http://www.mnd.uscourts.gov/MDL-Fidelis/Orders/2009/090105-08md1905ord.pdf.)

4. Makower J, Meer A. FDA Impact on U.S. Medical Technology Innovation. A Survey of Over 200 Medical Technology Companies. November 2010.
5. Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry. California Healthcare Institute. The Boston Consulting Group. February 2011.
6. Cohen D, Billingsley M. Medical Devices: Europeans are left to their own devices. BMJ 2011;342:d2748 doi: 10.1136/bmj.d2748.

Mr. STEARNS. I thank you, and I thank all our witnesses.

Dr. Ianchulev, you mentioned a capital report in your testimony. Do you mind submitting it for the record?

Mr. IANCHULEV. I have it here.

Mr. STEARNS. OK. That would be fine.

Let me start by asking my questions. Dr. Fischell, I will start with you. Your résumé obviously is very impressive. You are a physicist, an inventor. It says you have over 200 U.S. and foreign medical patents. At one time you were honored as inventor of the year in the United States, so you do have a high degree of credibility. So my question to you is, you state in your testimony that the environment that exists today at the FDA device center over the past few years, you specifically pointed out, is the worst that you have experienced in 42 years. Now, that is a pretty strong, dramatic statement. Can you give us specifics why you think that is true?

Mr. FISCHELL. There is a new attitude of the reviewers at the FDA. They are very proud to be conservative. Conservative says oh, I am going to throw it back, I won't approve it, therefore, I am protecting the American people from potential harm, and in some cases, they should have. One of the problems is that the reviewers are not expert in the field. For example, with our migraine device, we proved in clinical trial it cured migraine, it cured sensitivity to light and sound, but we didn't reach the 95 percent certainty for nausea, only 88 percent certainty. They said it is therefore not approvable for pain, for migraine, which it cured in an excellent way. So I think it is this conservativeness that the people have that is encouraged and say oh, you are really a good guy, and to me, that is the main problem. I think we need more expertise at the reviewer level. We have a medical advisory board of eight leading migraine doctors in the world who go to the FDA and say what should be approved. The person there is a couple months out of college with no training in migraine and they stop it.

Mr. STEARNS. Dr. Shuren is here in the audience, and I want to compliment him for staying and listening here. Normally sometimes the Administration speaks first. He was very confident and conscientious enough to say he would listen to you, so I think that is a credit to him, and I want to compliment him for staying and listening. Oftentimes the Administration comes over and speaks and they are out the door. So it is a compliment to him for staying here.

But let us I put you in charge of FDA tomorrow, oK? What would you do different or what would you tell Dr. Shuren that you would suddenly create this new environment that would give the United States the answer to some of these problems that our witnesses have said?

Mr. FISCHELL. I would—I have carefully thought about this and the problems that Congressman Waxman has raised, and what I think should be done is, when a 510(k), for example, goes to the FDA, the reviewer then should seek like three experts in that field to review the clinical trials suggested, and when that clinical trial is done, to review the results so that it is reviewed by people expert in the field, not just a reviewer with no experience in that field. I think that would change safety and efficacy.

Mr. STEARNS. So the bottom line is that people that are making these decisions don't have the confidence, in your opinion?

Mr. FISCHELL. I was with Commissioner Hamburg just a couple of weeks ago, who said they have a lot of trouble with retaining people and what have you, and I think that the FDA could easily call upon within a week of submission experts in the field like three experts in leads for defibrillators, and say please review this because you have spent 10 years of your life on it, I have never heard of it before. Does it not seem obvious that those who are expert in the field should be reviewers, not a person who happens to be there?

Mr. STEARNS. But it is interesting, you are saying that in your 42 years of experience, you have never seen it as recent in the last couple years like it is today, so your complaint is very serious on criticism of the present FDA right now.

Mr. FISCHELL. I think there is a different attitude there than we have seen before.

Mr. STEARNS. Thank you for saying that.

Dr. Ianchulev, Dr. Shuren, who is behind you, mentions in his testimony that poor submission quality is a big reason behind the sharp increase in review times we have seen in the past 7 years. That is going to be his case. Now, you have a lot of experience in submitting device applications to the center. Do you agree with his assessment?

Mr. IANCHULEV. Yes. I can make a comment on that. It is always hard to be self-critical. I am sure my submissions can probably be better, but a couple of observations that I have realized working on that front in the trenches. Very often, as we know, companies that operate in the device space especially and it is slightly different in the drug space with the big pharmaceuticals are smaller companies, companies that have fewer than 50 employees, so one can imagine that they don't have always in-house expertise and specialization. But at the same time, a lot of them outsource all of their regulatory processes, especially today when they are so challenged and so complex, they outsource it to regulatory experts, and in my experience, that has been usually the way of submissions to the FDA to go through an outside consultant or expert with usually 20-plus years of regulatory experience. So I really can't comment to every submission. I am sure that they have better visibility to that but I can imagine that that expertise on the consulting firm has not changed.

And then also, I think that is a good point because it would be really nice to see best-in-class examples of submissions where the agency proactively can give that guidance if they are concerned about the status and quality of those submissions, that people that work with them can see what the expectations are up front, see good examples of good submissions and really adjust their practices.

Mr. STEARNS. I thank the gentleman. My time is expired.

The gentlelady from Colorado, Ms. DeGette, the ranking member, is recognized for 5 minutes.

Ms. DEGETTE. Thank you very much, Mr. Chairman. I want to thank all the witnesses for coming today and particularly the three patient advocates who have come their stories.

I just want to clarify with all three of you. Your stories are all compelling and they touch all of us because we all have relatives or friends in the same situation. By talking about how these devices could be brought to market and help you or your families, none of you are saying that you would sacrifice safety or thoroughness of review, correct? Ms. Murphy, you're not saying you would sacrifice safety or thoroughness of review?

Ms. MURPHY. No, I am not.

Ms. DEGETTE. And Ms. Conger?

Ms. CONGER. Safety and what?

Ms. DEGETTE. And thoroughness of review to make sure that it is safe.

Ms. CONGER. Within reasonable.

Ms. DEGETTE. Right. Ms. Sagan?

Ms. SAGAN. Absolutely.

Ms. DEGETTE. You would not sacrifice——

Ms. SAGAN. I would not sacrifice safety.

Ms. DEGETTE. And Dr. Fischell, you are not saying that either. You think that these devices should be safe, correct?

Mr. FISCHELL. Absolutely, but it should be done in a timely manner.

Ms. DEGETTE. In a timely and efficient manner.

Now, Dr. Fischell, I don't know if you were aware, you are an inventor and you submit these devices to the FDA. Now, the budget that was passed by the Republican majority in the House two times this spring cut the FDA's funding by about $241 million. So if we are going to hope to be able to hire experts to review these applications quickly and to have the expertise, do you think that a substantial cut in the FDA budget would assist us in being able to expedite these reviews?

Mr. FISCHELL. I am sure that every company involved including about six companies I am involved with would be happy to pay for the fees paid to such experts to do the job in a prompt way.

Ms. DEGETTE. Right, but certainly budget cuts is not going to help us, is it?

Mr. FISCHELL. No, but the budget—this would not increase the budget.

Ms. DEGETTE. Right.

Mr. FISCHELL. It would be paid for by the——

Ms. DEGETTE. OK. I actually kind of agree with that.

Let me ask you, Ms. Sagan, because you mentioned the Special Diabetes Program, which makes funds available for type 1 diabetics and also American Indian populations, and last year we reauthorized that. As you said, a lot of those funds are going toward clinical trials for the artificial pancreas. Now, just so you know, we sent that letter that I mentioned that almost all the members of this subcommittee including the chairman signed asking about quick approval of the artificial pancreas, and also I spoke with Commissioner Hamburg about this issue of the low blood glucose, and I am pleased to tell you that we got a quick response to that letter in June and the FDA issued a guidance on that low blood glucose monitor stopping, so we can move forward on these things and we do have hope that we will move quickly.

But from your perspective and from your daughter's perspective, I know you probably agree, we don't want to approve an artificial pancreas if it is going to be defective because it could kill the patients, right?

Ms. SAGAN. Yes.

Ms. DEGETTE. So we want to make sure it is going to work.

Ms. SAGAN. Yes, we do.

Ms. DEGETTE. Yes. And that is kind of the same way I feel too. So I guess I wanted to ask you, what is your perspective as an advocate of how the FDA should balance the safety with the speed in approval that we need for these medical devices?

Ms. SAGAN. Well, in terms of the low-glucose suspend, I don't think there is an issue with safety.

Ms. DEGETTE. I agree with you on that, but in general——

Ms. SAGAN. In general, if—I mean, I believe that there should be clear guidance documents and a decision made in a timely manner. If it is a 90-day period, it should be 90 days, and it shouldn't be further delayed after that. We have to have safety and we are so ready to go to outpatient clinical trials with artificial pancreas. We have done all the inpatient clinical trials.

Ms. DEGETTE. Now, Dr. Curfman, I just want to finish with you because you heard all of these stories, and in your job you do all the time. What can be done to make sure that we expedite safe and efficacious devices but at the same do the thorough reviews that we need? Is there something that can be improved at the FDA right now to do that?

Mr. CURFMAN. We are looking for a balance. It has to be a balanced approach. On the one hand, we want to speed innovation to patients, absolutely. On the other hand, we want to be sure that the devices work, that they actually improve human health and that they are safe.

Ms. DEGETTE. Do you think there is any problem at the FDA right now?

Mr. CURFMAN. I think that there are two things that I would look at at the FDA. Number one, I do think that the 510(k) process needs to be looked at. I think there are issues there. Some devices are being looked at under the 510(k) that probably shouldn't be. On the other hand, there are also inefficiencies in the process that are slowing down approval in some cases. My sense is that it has gotten better but I think that more work can be done to make it a more efficient process.

Ms. DEGETTE. Thank you very much.

Mr. BURGESS. [Presiding] I thank the gentlelady for yielding.

Dr. Fischell and Dr. Curfman, let me just be sure I have some of my facts straight. Dr. Fischell, do I understand that you are affiliated with Johns Hopkins University?

Mr. FISCHELL. I worked at the Johns Hopkins University for 30 years and was on the medical faculty as well as working as a physicist at the Applied Physics Lab.

Mr. BURGESS. So an academic at Johns Hopkins?

Mr. FISCHELL. Yes.

Mr. BURGESS. And Dr. Curfman, are you at Mass General? Where is your hospital affiliation?

Mr. CURFMAN. Yes, at Mass General Hospital and Harvard Medical School.

Mr. BURGESS. So just on the face of it, it seems like the two of you are terribly similar. It appears as if your politics are similar, you are both academics at big Eastern facilities, and yet your conclusions are significantly different, at least as I perceive on the panel today. You are shaking your head no, you feel exactly as Dr. Fischell does. Is the difference because he is an innovator and you are a reviewer? I know in my days in medicine, we used to regard that there were two types of doctors. There are thinking doctors and there are doing doctors. As an OB/GYN, I was a doing doctor, all kinds of things we did in our practice, but I didn't think very much. So you are the thinking doctor here, and Dr. Fischell is the doing doctor. Is that the difference here?

Mr. CURFMAN. No, I think we are really on the same page but innovation requires two things. It requires fresh ideas, new ideas, interesting new approaches, but it also requires careful testing to be sure that the device works.

Mr. BURGESS. And I don't disagree with that. I want to get back to the 510(k) process in a minute, but Dr. Fischell, you said something that I just thought was so important. I mean, in this committee in 2007, we reauthorized the user fees for both the prescription drugs and medical devices here in this committee, and one of the big fights that we had that I lost was over the people that make up these advisory panels to the FDA, and at that time, of course, Republicans were not in charge and that is why I lost, but the pendulum swung so far that we cannot have anyone on a review panel that might have any appearance of a conflict of interest, and as a consequence, we excluded the universe of people who actually had some idea about what these products did. So in retrospect, I guess what I am trying to get you to say that I was right with those amendments that were defeated, but can you speak to that for just a moment? Because you were on that path a moment ago.

Mr. FISCHELL. Yes.

Mr. BURGESS. And I want former Chairman Waxman, Ranking Member Waxman to hear this.

Mr. FISCHELL. Well, there is always——

Mr. BURGESS. So start out with "Dr. Burgess, you were correct."

Mr. FISCHELL. Yes, I do believe you are correct, and even though I am a very good friend of Congressman Waxman, and it is a matter of, there is an old saying, you can either have somebody who is expert in it and they—or someone who has never worked in the field, and if you have someone who has no knowledge of the field, that doesn't work very well. And so you need people who really have knowledge in that field, and also the FDA seems to be exceedingly slow. They don't even follow their own guidelines. For example also, in this device for migraine, there is no predicate device. We invented something new. And so we had to go to a 510 de novo 510(k). To get a de novo 510(k), you must first say to the FDA that we cannot find—no, we first suggest devices that could be predicate devices. We knew there were none. And they said you are wrong, there are none. We say it is de novo. They said oh, oK, then it can be de novo. You cannot go to the FDA and say it is a de novo device.

Mr. BURGESS. Do you think——

Mr. FISCHELL. That cost us several months at the beginning.

Mr. BURGESS. Do you think you got good advice from the FDA about what they would need to see from you to get this device approved in a reasonable period of time?

Mr. FISCHELL. No. We wanted to cure migraine headache. They needed us to cure photophobia, phonophobia and nausea with a 95 percent certainty.

Mr. BURGESS. Let me ask you a question on the nausea.

Mr. FISCHELL. We got 95 percent on two of them but only 88 percent in nausea and they therefore said, I will never forget the words, it is not approvable.

Mr. BURGESS. On the nausea question, does a placebo score an 88 percent if you——

Mr. FISCHELL. No, no, no. We were much better than the placebo but so few patients had nausea that we didn't get the statistic.

Mr. BURGESS. And this is a noninvasive device?

Mr. FISCHELL. Correct, and not only that——

Mr. BURGESS. You don't have to open anyone's head and put anything inside?

Mr. FISCHELL. A prior device made by Neuronetics for depression has 20 percent stronger magnetic pulse and 30,000 times more pulses. It is approved and working by the prior FDA. Even though we were a tiny fraction of that, we could not gain approval.

Mr. BURGESS. Let me just, Mr. Mandel, if I could, just ask you briefly on the MelaFind. In the continuum of things that are approved, where does MelaFind fall? Is it a reasonable device for a practicing physician to have in their hands?

Mr. MANDEL. I think the company is intending it to be an adjunct for dermatologists, so I think you have to distinguish between the first-generation device, which would be restricted, I think, to experts with a lot of savvy, and then the company wouldn't say this but I would, if you kind of look down the path future in the future, you could see how the improvements would enable that it could be more used more broadly than that, and when I think about what is being lost right now, it is not only the device as it exists but it is the future as well.

Mr. BURGESS. Well, I would just say from the perspective of somebody who used to practice general OB/GYN, to have a device, we are told we must do skin screenings every year when a patient comes in for a visit to have something that could help us determine, rather than just sending everything back to the dermatologist or off to the dermatologist to be biopsied at great cost, something to help us discriminate a little bit finer because not all of us remember what we learned in medical school about the irregular borders, the degree of coloration.

Mr. MANDEL. The FDA says it wants to have a device. The FDA says that it wants the device to be able to do that, to be able to help an inexperienced doctor, but there is no way to get from here to there without the steps in between. It is like asking—it is like refusing to approval the initial cell phone until you can have an iPhone first.

Mr. BURGESS. I understand. Well, I thank you, and I will yield back my time and yield to Mr. Waxman for questions.

Mr. WAXMAN. Thank you very much. Thank you all. As witnesses, you have been very compelling in your stories and your experiences, and all of us want to see these things move faster. We want to get those therapies to those who need it. The question that comes to my mind, the proposals that would weaken the standards for the Food and Drug Administration, I think a lot of the problem, and I look forward to hearing from Dr. Shuren after this panel, but I think a lot of the problem is that either the FDA does not have the resources or there are problems at FDA in processing what is going on or there are problems with the developers, the manufacturers who aren't getting their studies done adequately. And I must say, when I hear about weakening the standards, it bothers me because we hear all the time reports about horrific patient suffering from dangerous medical devices. In the last year, the New York Times reported on radiation machines that have killed and disfigured patients, malfunctioning linear accelerators that left a woman nearly comatose. We have heard from the father of a patient who died due to an overdose of radiation therapy, and we have also heard about problems with the Sprint Fidelis implantable heart devices that caused at least 12 deaths. I don't think devices are something that we shouldn't take seriously as we do drugs. They both must meet a safety and efficacy standard. In the face of these reports of problems, it is hard to agree with the sentiment that we need to reduce FDA's authority to make sure medical devices are safe and effective.

Dr. Curfman, you testified on this subject. Should we be looking at strengthening or weakening FDA's standards and FDA authority for medical device approval?

Mr. CURFMAN. Thank you. It is a balance. We all want devices to move quickly to patients so that our patients are helped by them but at the same time they need to be evaluated, and the clinical trial, the randomized clinical trial is now the gold standard for evaluating drugs and devices, and we are very fortunate in our country to have some of the leading clinical trial centers in the world in the United States. This has become a very expert scientific discipline to run a good clinical trial, to do it right, to do it rigorously, to get the right answers. And we are very fortunate now that this science of doing clinical trials has become very, very sophisticated. We have in the United States among the very best clinical trialists in the world and they understand the importance of doing these trials efficiently and quickly, and we at the New England Journal understand the importance of publishing the results of these trials quickly and efficiently.

Mr. WAXMAN. We had problems with drugs, and the concern about the delay of approval of drugs, so a number of years ago when I was chairman of this subcommittee, we put into law that there would be a user fee that the manufacturers of the pharmaceuticals would pay so that FDA could hire the personnel. I don't like that idea. I think this is a government function and we ought to be willing to pay for essential government functions, and the FDA is one of those essential government functions. But there was no way we were going to get more appropriations.

Now, in the medical device area, we do not have a user fee. We are relying on the money that the government appropriates for

FDA. I would be interested if anybody on this panel thinks it is appropriate, given your concerns, that we reduce FDA's money. I think the Republicans are proposing to reduce FDA by $250 million, which would make them less able to approve drugs and devices and to do the other things that they need to do like food safety. Does anybody think it is a good idea to reduce the funding for FDA?

Ms. CONGER. Yes, I do, because I don't think that the FDA, the organization as itself is functioning as efficiently as it could be because——

Mr. BURGESS. Well, you think they should be——

Ms. CONGER [continuing]. They drag——

Mr. BURGESS. I only have a limited time. So you think they should be because FDA is not doing a good job. I want FDA to do a good job, but FDA has to have the resources. There is a user fee and there is a fight——

Ms. CONGER. And the right people.

Mr. BURGESS. They need the right people. They need to pay the right people. You are not going to get good, competent people to work for the government if you underpay them.

Ms. CONGER. And don't——

Mr. BURGESS. Excuse me. I am not in a conversation.

Ms. CONGER. I am sorry.

Mr. BURGESS. Perhaps another time. But the fact of the matter is, proposals are to weaken the standards, spend less money on the FDA, and all this has to be put in the perspective of the Supreme Court decision that I think was misguided when they said some medical devices are immune from lawsuits at the State level.

Dr. Curfman, do you have any view on the Supreme Court decision preempting lawsuits at the State level?

Mr. CURFMAN. Well, it is pretty irrational because there is a different standard for drugs and devices. There is preemption of State-level legal action for devices. There is no preemption of State legal action for drugs. So it just doesn't make any sense. There may be technical legal reasons why it came out that way but we need to do something about that to make this a more rational and logical system.

Mr. WAXMAN. Well, I just want to say in closing, I don't think we are going to be moving in the right direction if we reduce the money that goes to FDA, we don't get a user fee to help them pay for the people reviewing the medical devices, and then the answer isn't to say oh, just put them on the market and we will see what happens. If people get hurt, they won't use them anymore. If they are hurt because of negligence, they can't sue. And then the FDA can't even conduct the oversight on the safety and the efficacy of these products.

I know my time is expired. The chairman has been as generous to me as he was to himself, and I thank him for it.

Mr. BURGESS. And I thank the gentleman for recognizing that. I will also point out that Dr. Sharfstein was here before our committee last year and testified that they didn't need any more money, they had plenty.

Let me yield to Mr. Terry from Nebraska for questions.

Mr. TERRY. Thank you.

First, I mean, we on our side have been in discussions about FDA and these delays. I haven't heard any of us talk about weakening the standards, so I am sorry, I don't know where that is coming from. We are frustrated that FDA has become—the delays have become so difficult for the inventors and manufacturers that they feel that they have to set up shop in Europe in order to proceed. So we are trying to work through that, Dr. Curfman. I don't know where you came up with the idea or you and Henry Waxman that we are weakening.

But Ms. Conger, I felt badly the way that you were treated. A question was thrown out that you weren't allowed to answer. If you would like to use a little bit of my time to answer the question?

Ms. CONGER. The question about?

Mr. TERRY. Mr. Waxman's about funding.

Ms. CONGER. The funding, yes. I have been in business, and I have seen organizations that stagnate and stagnate, and the big kahunas on the top can't understand why their brilliant ideas aren't filtering down into the little plants and the roots and why aren't they going, and it is very simple. It is that you do what you get rewarded for. You do the things you don't get in trouble for. And while we may have some very, very fresh ideas and even some of the things that I brought up, we still have an old, ingrained guard that has been taught to keep your head low and just keep doing it the old way, and the FDA CDRH can no longer afford to do it the old way. They have their competitors in other nations who are already bringing them tons of data about products that are successful in millions of patients——

Mr. TERRY. Ms. Conger, that is a really good point there.

Ms. CONGER. Yes.

Mr. TERRY. And one that——

Ms. CONGER. And then start them all over again. Excuse me.

Mr. TERRY. Dr. Curfman, you are the defender here of the status quo of the FDA.

Mr. CURFMAN. No, no.

Mr. TERRY. So let me ask you this. Well, hold on. Her point is one that is going through my mind, and let us use the low-glucose suspend system where the conclusion of this mother, Ms. Sagan, is that low-glucose suspend systems have been approved for nearly 3 years and used safely all over, 40 countries worldwide, but they are not available here. It seems to me that our FDA refuses to acknowledge results and data from other countries on the same device. Is that an appropriate standard? Is that appropriate?

Mr. CURFMAN. Well, Mr. Terry, let me just comment about my own interaction and experience with the FDA. I know many people——

Mr. TERRY. Would you answer my question?

Mr. CURFMAN. Yes, I am answering it. I know many people who have served on advisory committees to the FDA and they are highly expert. They are the best experts in the world. They are providing the very best advice that the FDA can get, the best advice anywhere in the world, and in the end, decisions about what devices are going to put in the market have to be based on evidence, not on feelings, not on impressions.

Mr. TERRY. So are you saying that the—feelings and not real data?

Mr. CURFMAN. Data from anywhere needs to be judged on its merits, and that is what advisory committees do, and that is why the FDA brings in the very best people from the medical community, the scientific community——

Mr. TERRY. And start all over.

Mr. CURFMAN [continuing]. And make these judgments, and to evaluate the clinical trial data——

Mr. TERRY. With my 48 seconds, let me ask you——

Mr. CURFMAN [continuing]. And to see if it really supports——

Mr. TERRY. Well, I appreciate you trying to run out the clock here, but you were very critical of the European system of approval. Can you detail their inadequacies?

Mr. CURFMAN. Sure. I have several concerns about it. First of all, as you know, Mr. Terry, the European system is based on 76 private bodies, 76 in Europe, six in the UK, that make the decisions about which products go on the market. So it is very diverse. It is very spread. It is not a unified process. And there is a lot of inconsistency among these 82 private bodies that make these decisions. So that is one concern that I have: inconsistency of standards across all of these regulatory bodies.

Secondly, there is very little or almost no transparency to the approval process in Europe. The FDA has a beautiful Web site. All of the information about new devices and drugs is available there. Anybody can find it. It is available to the public. This is not true in Europe, and if you try to get information in Europe, they tell you that is proprietary and you can't get it.

Third, and I think of most concern, in Europe, for class III devices, these are the most complex medical devices, it is not necessary to show that that device is going to improve a person's health before it goes on the market. That is of great concern to me. We are living in an era now where outcome-based medicine is what it is all about. This is core to medicine and health today, to show that something improves a person's health, and that isn't a requirement for putting a device on the market in Europe. I think that is of great concern.

Mr. BURGESS. The gentleman's time is expired, and I see several people have their hands up, but we do need to go to the chairman emeritus of the full committee, Mr. Dingell, for questions.

Mr. DINGELL. Thank you very much, Mr. Chairman. My questions are going to require yes or no answers, and I am sorry about that but there is a very limited amount of time and a lot of questions to be asked.

These questions will go to Dr. Curfman. Your testimony references two examples of innovative devices that were approved without a clinical trial. As you know, new drug applications require clinical trials for approval. Do you believe that the two examples referenced in your testimony were inappropriate for the 510(k) process? Yes or no.

Mr. CURFMAN. Yes.

Mr. DINGELL. Now, Doctor, there have been reports of some class III devices being reclassified as class II devices, allowing them to gain approval through the 510(k) process without need for clinical

trials. In your work at New England Journal of Medicine, have you found this to be a common industry practice? Yes or no.

Mr. CURFMAN. Yes.

Mr. DINGELL. Doctor, as you know, class III devices are devices by their nature that should require a stricter review by FDA. These devices are often necessary to sustain the life of a patient and are in some instances implanted into the patient's body. Is it true that a device that goes through premarket approval process can be approved based on a single clinical study? Yes or no.

Mr. CURFMAN. Generally, no.

Mr. DINGELL. Should they be approved on the basis of a single clinical trial?

Mr. CURFMAN. No.

Mr. DINGELL. Do you believe that the clinical trial standards laid out by FDA in the premarket approval process are rigorous enough to prove safety and effectiveness of class III devices? Yes or no.

Mr. CURFMAN. Most often, yes.

Mr. DINGELL. Do you believe that a single study is sufficient to approve a class III device? Yes or no.

Mr. CURFMAN. No.

Mr. DINGELL. As you know, device manufacturers are required to conduct postmarket surveillance. Do you believe that the current postmarket surveillance requirements are adequate? Yes or no.

Mr. CURFMAN. No, but they are getting better.

Mr. DINGELL. So you think that is something we ought to have a look at?

Mr. CURFMAN. Indeed.

Mr. DINGELL. Now, Doctor, do you believe that the device manufacturers have met their responsibility to conduct rigorous postmarket surveillance to ensure the safety of their devices? Yes or no.

Mr. CURFMAN. No, that is a big problem.

Mr. DINGELL. Your testimony references the EU medical device approval process and the timelines to approval are only modestly shorter in the EU. How much shorter is the timelines for approval? Can you give us some kind of a horseback guess on that?

Mr. CURFMAN. Depending on what you are measuring, it can be a few months to a year. In the lifespan of a drug or a device, that is a small fraction of the total.

Mr. DINGELL. Now, as you know, the standards for approval in the United States and EU are different. Do you believe that the EU approval process adequately takes into consideration the success of a device in treating a patient? Yes or no.

Mr. CURFMAN. No.

Mr. DINGELL. Do you believe that the approval process in the EU is transparent to the public when approving devices for use? Yes or no.

Mr. CURFMAN. No.

Mr. DINGELL. Should be more transparent, should it not?

Mr. CURFMAN. Much more transparent, yes.

Mr. DINGELL. Thank you very much for this. This goes to Dr. Fischell and Dr. Ianchulev. I would like to end my questions with you regarding your experience with FDA regarding the medical device approval process. Please again answer yes or no. Are you

working with the FDA review staff and the approvals of your device? Did you find that the FDA review staff was responsive to questions or concerns? Yes or no.

Mr. FISCHELL. No.

Mr. DINGELL. Now, were the requirements for the approval of your device made clear to you by the FDA review staff in the beginning? Yes or no.

Mr. IANCHULEV. No.

Mr. FISCHELL. No.

Mr. DINGELL. Have you found the review process to be consistent? Yes or no.

Mr. IANCHULEV. No.

Mr. FISCHELL. No.

Mr. DINGELL. Do you believe that the review staff at the FDA are adequately trained to review the devices based on the most up-to-date science? Yes or no.

Mr. IANCHULEV. No.

Mr. FISCHELL. No.

Mr. DINGELL. Now, I would just like to comment in the 26 seconds left to me, Mr. Chairman.

Mr. STEARNS. Will the gentleman yield just for question? You might want to give them a chance to—it looked like some of them didn't have a chance to answer.

Mr. DINGELL. My time is running.

Mr. STEARNS. OK. No problem.

Mr. DINGELL. My time is running, Mr. Chairman.

Way back, we had a nasty experience in this country. It related to a substance which caused problems with regard to babies given to mothers for morning sickness. It was approved in Europe but it was not approved over here. It resulted in a whole big change in our food and drug laws, and it was a matter of very special concern. The precise name of the pharmaceutical, I don't remember.

Mr. FISCHELL. Thalidomide.

Mr. DINGELL. Thalidomide. Thank you very much. It caused a huge stir and a tremendous amount of difficulty because of the way the Europeans went into these matters as opposed to the way that we went into them, and I am very loathe to see us weakening our laws to simply carry forward the goals of the Europeans, who occasionally make mistakes too.

Mr. Chairman, you are most gracious. Thank you.

Mr. STEARNS. The gentleman yields back.

I would like to put into the record—the gentlelady, the ranking member, has asked the supplemental memorandum July 20th be put into the record. By unanimous consent, so ordered.

[The information follows:]

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED TWELFTH CONGRESS

Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115

Majority (202) 225-2927
Minority (202) 225-3641

SUPPLEMENTAL MEMORANDUM

July 20, 2011

To: Democratic Members of the Subcommittee on Oversight and Investigations

Fr: Oversight and Investigations Democratic Staff

Re: Supplemental Information on "Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation, and Jobs."

On Wednesday, July 20, 2011, at 10:00 a.m. in room 2322 of the Rayburn House Office Building, the Subcommittee on Oversight and Investigations will hold a hearing titled "Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation, and Jobs." The majority has indicated that the hearing will focus on the state of the medical device industry and the impact regulations and policies at the Center for Devices and Radiological Health have on patient access, innovation, and job creation.

Committees in both the House and Senate, including the House Committee on Energy and Commerce, have recently held hearings on FDA regulation of medical devices. During these hearings, proponents of a weaker regulatory regime have repeatedly referred to two reports to claim that FDA's medical device clearances and approvals are slower than those of the European Union.[1] The first report is titled *FDA Impact on U.S. Medical Technology Innovation* and was written by Dr. Joshua Makower and co-authors.[2] The second report is titled *Competitiveness and*

[1] See, e.g., Reps. Pitts, Upton, Lance, and Blackburn, House Committee on Energy and Commerce, *Impact of Medical Device Regulation on Jobs and Patients* (Feb. 17, 2011); Reps. Pitts, Burgess, Blackburn, House Committee on Energy and Commerce, *PDUFA V: Medical Innovation, Jobs and Patients* (July 7, 2011).

[2] Makower, J., Meer, A., and Denend, L., *FDA Impact on U.S. Medical Device Technology Innovation* (Nov. 2010) (online at www.inhealth.org/doc/Page.asp?PageID=DOC000188) (accessed on July 19, 2011).

Regulation: The FDA and the Future of America's Biomedical Industry and was written by the California Healthcare Institute and co-authors.[3] Both studies were funded by the medical device industry and neither was published in a peer-reviewed journal.

To determine whether these studies form an appropriate basis for policymaking, the Democratic staff of the House Committee on Energy and Commerce requested their review by three editors of the premier peer-reviewed medical journals in the United States: Dr. Gregory Curfman, Executive Editor of New England Journal of Medicine; Dr. Rita Redberg, Editor-in-Chief of the Archives of Internal Medicine; and Dr. Howard Bauchner, Editor-in-Chief of the Journal of the American Medical Association. At the staff's request, officials from FDA also submitted comments on the studies.[4]

I. KEY FINDINGS

All three independent reviewers and the Food and Drug Administration identified major problems with both studies, raising significant questions about their methodologies and their appropriateness for serving as the basis of new policies governing the medical device approval process.

A. Makower Study Findings

Dr. Makower and his co-authors based his findings on a survey of medical device firms and concluded that "data from the survey clearly indicate that European regulatory processes allow innovators to make new medical technologies available to patients more quickly and at a lower cost."[5] One industry group stated: "This powerful study provides compelling evidence of

---

[3] California Healthcare Institute and the Boston Consulting Group, *Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry* (Feb. 2011) (online at www.bcg.com/documents/file72060.pdf) (accessed on July 19, 2011).

[4] The Democratic staff of the House Energy and Commerce Committee posed the following questions: (1) "What would you identify as the major methodological issues (whether positive or negative) of this study?"; (2) "Specifically [for the Makower study], can you comment on the response rate for the survey overall, and for the subgroup regarding the time to first contact?"; (3) "Do you have any views on the methodology used in the study to compare E.U. and U.S. approval times?"; (4) "Would you recommend publication of this study in a peer-reviewed journal?"; and (5) "Are there issues not addressed at all in this study that might be helpful in a comparison of the EU and US?" Dr. Bauchner declined to provide comments on the CHI study, citing a conflict of interest.

[5] Makower, J., Meer, A., and Denend, L., *FDA Impact on U.S. Medical Device Technology Innovation* (Nov. 2010) (online at www.inhealth.org/doc/Page.asp?PageID=DOC000188) (accessed on July 19, 2011).

what we have been hearing for years . . .: the current regulatory environment is adversely impacting innovation, patient care and job-creation here in the United States."[6]

Dr. Makower testified that "the study found that for low- and moderate-risk devices, the process to navigate the FDA took companies up to two years longer than it did for a similar approval from European regulators. For higher-risk devices, the discrepancy was greater -- in the U.S., it took three and a half years, or five times as long as Europe, to grant approval."[7]

Dr. Makower sent his survey to approximately 750 potential participants. Of these, only 204 responded. Dr. Makower used the experience of 15 of these respondents to conclude that the medical device approval process takes 31 months under the FDA's 510(k) notification program in contrast to just seven months for medical device approval under the European Union system.[8]

The reviewers identified numerous methodological flaws in the study. These include:

- The existence of "so many flaws in design and execution that the authors' conclusions are rendered essentially meaningless."[9]
- A "woefully inadequate" response rate of only 20%.[10]
- A biased group of respondents including firms that "had never gone through the process of getting a product reviewed by the FDA."[11]
- A "subjective,"[12] "apples to oranges,"[13] and "especially troublesome"[14] comparison of approval times in the European Union and the FDA.

---

[6] Medical Device Manufacturers Association, *Powerful New Study Details the FDA Role in Med-Tech Innovation* (Nov. 18, 2010) (online at www.medicaldevices.org/node/846) (accessed on July 19, 2011).

[7] House Committee on Energy and Commerce, Testimony by Dr. Joshua Makower, *Impact of Medical Device Regulation on Jobs and Patients* (Feb. 17, 2011).

[8] *Id.*

[9] Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[10] *Id.*

[11] Letter from Jeanne Ireland, Assistant Commissioner for Legislation, U.S. Food and Drug Administration, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011).

- The failure to provide "any evidence that this [U.S.] delay or lack of availability leads to adverse health outcomes."[15]

After reviewing the paper, the editors of the three premier peer-reviewed medical journals concluded that the study would not be fit for publication in a peer-reviewed journal. Dr. Curfman concluded that "it is not really a study at all."[16] Dr. Redberg found "several serious methodological issues with the Makower report that render its findings scientifically invalid."[17] Dr. Bauchner determined that "[g]iven the extent of these limitations, the inferences and conclusions that can reliably drawn from this report are limited.[18] Finally, all three editors identified significant conflict of interest concerns with the report.[19]

---

[12] Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[13] Letter from Jeanne Ireland, Assistant Commissioner for Legislation, U.S. Food and Drug Administration, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011).

[14] Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[15] Letter from Howard Bauchner, M.D., Editor-in-Chief, JAMA and Scientific Publications, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011).

[16] Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[17] Letter from Rita F. Redburg, M.D., MSc., Chief Editor, Archives of Internal Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[18] Letter from Howard Bauchner, M.D., Editor-in-Chief, JAMA and Scientific Publications, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011).

[19] Letter from Howard Bauchner, M.D., Editor-in-Chief, JAMA and Scientific Publications, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011); Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011); Letter from Rita F. Redburg, M.D., MSc., Chief Editor,

B. CHI Study Findings

The study by the California Healthcare Institute examined both drug and device approvals. The findings on device approvals were based on FDA's device approval databases and other data sources. This study concluded that device approval times had increased, that approval times in the European Union were faster than those in the U.S., and that "inefficiency at the FDA has resulted in American inventions being made available to patients and physicians in other countries first . . . [and] has pushed jobs and revenues offshore."[20]

Reviewers identified numerous problems with this study, including:

- The paper "reflects little or no understanding of the complexity of medical devices and the sometimes unpredictable adverse health consequences of seemingly minor changes in design."[21]
- The report "is written exclusively from the business perspective and does not address the important medical or public health dimensions of medical devices."[22]
- The use of an "'apples to oranges' comparison [between U.S. and E.U. review times] that does not take into account the difference in the review standards between the two regulatory regimes."[23]
- The text of the report fails to mention that "about 80 percent of the devices [FDA] review[s] premarket, come on the market in the United States first as often or more often than in the EU."[24]

Archives of Internal Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[20] California Healthcare Institute and the Boston Consulting Group, *Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry* (Feb. 2011) (online at www.bcg.com/documents/file72060.pdf) (accessed on July 19, 2011).

[21] Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

[22] *Id.*

[23] Letter from Jeanne Ireland, Assistant Commissioner for Legislation, U.S. Food and Drug Administration, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011).

[24] Letter from Jeanne Ireland, Assistant Commissioner for Legislation, U.S. Food and Drug Administration, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 18, 2011).

- The study "assumes the faster the FDA approves a device, the better. That may be true from the perspective of a medical device company, but it is not true from the perspective of patients."[25]

Dr. Redberg determined that "[d]ue to the methodological limitations and faulty assumptions described above, it is my opinion that this study would not be accepted in a peer-reviewed medical journal."[26] Dr. Curfman concluded: "[T]hese two reports together do a serious disservice to medicine and the health of the public."[27]

[25] Letter from Rita F. Redburg, M.D., MSc., Chief Editor, Archives of Internal Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 17, 2011).

[26] *Id.*

[27] Letter from Gregory D. Curfman, M.D., Executive Editor, New England Journal of Medicine, to Henry A. Waxman, Ranking Member, House Committee on Energy and Commerce (July 15, 2011).

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL OFFICES

July 15, 2011

The New England Journal of Medicine
10 Shattuck St., 6th Floor
Boston, MA 02115

The Honorable Henry A. Waxman
2204 Rayburn
House Office Building
Washington, DC 20515

Dear Congressman Waxman:

My name is Gregory Curfman, MD, and I am the executive editor of the *New England Journal of Medicine*. I am writing to provide you with commentary about two recent reports on the regulation of medical devices entitled, respectively, "FDA Impact on U.S. Medical Technology Innovation" and "Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry." I do so both because of my personal interest in medical device regulation and also because part of the medical journal I edit is focused on the publication of new research on medical devices.

The first report was written by two authors, Dr. Joshua Makower, who has numerous financial relationships with the medical device industry, and Aabed Meer, a medical student who has very little experience in medical research. It was surprising that Dr. Makower's financial relationships were not individually identified in the disclosure note in the report, since these relationships clearly constitute a significant conflict of interest on Dr. Makower's part in regard to this report. It appears from the disclosure note that the authors were paid by the Medical Device Manufacturers Association to prepare this report. If this is the case, it should be explicitly stated in the disclosure note, since this would constitute a conflict of interest with respect to this report.

Although the report refers to this work as a "study," it is not really a study at all. This is an opinion piece that is dressed up to look like a research study. In fact, there are so many flaws in design and execution that the authors' conclusions are rendered essentially meaningless. From the start, the authors had a specific agenda to reach particular conclusions, and they conducted the work in a biased manner that would give them the result that they wanted.

The 20 percent response rate of the medical technology companies surveyed is woefully inadequate. In contrast, we would never publish in our journal a survey that did not have a response rate of at least 60 percent or higher. The 20 percent of companies that did respond were clearly subject to substantial selection bias, i.e. those companies that were unhappy with the regulatory process at FDA were more likely to take the time to respond, thus biasing the results.

All of the numerical information was collected by telephone interview or in an online format. Of note, none of the information was independently validated by the authors. Ordinarily, in a rigorous study there should be validation of at least a subgroup of companies to ensure that the data they are reporting are accurate. The Methodology section of the report indicates that PricewaterhouseCoopers LLP verified the study results. However, it does not appear that the original data were independently verified through an audit to ensure their accuracy, and this is what would need to be done.

The conclusions about the comparison of US and EU approval times are especially troublesome. These conclusions were based solely on the subjective responses of the biased sample of survey respondents. The comparison of the US and EU does not include any formal assessment of the outcome of the regulatory procedures, especially whether the assessment of efficacy and safety were more complete and rigorous in the US. A valid comparative study of device regulation in the US and EU must include information about the outcome of the regulatory process, not just which agency was more "reasonable" in the eyes of the technology companies.

Finally, none of the quantitative data in the report include measures of variation in the data (such as standard deviations or confidence intervals), and most surprisingly there is no statistical analysis to assess the significance of differences.

Overall, this is a very unsatisfactory report that would not merit publication in a respected peer-reviewed medical journal.

The second report comes from the California Healthcare Institute, a policy-research and advocacy organization, and among its clients are medical device companies. The report is written exclusively from a business perspective and does not address the important medical or public health dimensions of medical devices. One part of the report is particularly revealing in this regard. In the section entitled "Regulatory Risk: Spotlight on the FDA," the report boldly notes that "From investors' perspective, regulation has always been a risk factor." The report attempts to paint regulation itself as a risk, and – astonishingly – leaves unmentioned the fact that the principal purpose of FDA regulation in the first place is to mitigate potentially serious risks to patients from ineffective or faulty medical devices.

Another part of the report discusses the 510(k) pathway for expedited approval of devices in which there has been only an incremental change in a previously approved device. One sentence reads: "Devices, in contrast, may be altered in minor ways – switching to a new

metal alloy, installing a longer-lasting battery, using a better polymer – so that the effects on the product's safety and efficacy profile are predictable." This sentence is particularly ironic in the light of the recent disaster involving metal-on-metal artificial hip implants. Hip implants originally consisted of a metal ball inserted into a plastic cup. In newer models the plastic was replaced by a metal alloy ("metal-on-metal" design), which was generally regarded as a major innovation. However, the implants did not undergo clinical trials before marketing, only bench testing. Not long after FDA approval, reports of failure of the metal-on-metal implants and shedding of metallic debris began to surface, and upwards of tens of thousands of patients have been affected. Thus, an apparently "minor" alteration in design – replacement of plastic with metal alloy – resulted in a public health nightmare.

This example highlights the naiveté of the report from the California Healthcare Institute. The report reflects little or no understanding of the complexity of medical devices and the sometimes unpredictable adverse health consequences of seemingly minor changes in design. In general, this report advocates a potentially dangerous position – that regulation stifles innovation – while in fact reasonable regulation is essential in order to avoid the lure of so-called "innovations" that may in fact result in unsafe or ineffective medical devices and adverse health outcomes for patients.

In summary, for the reasons discussed these two reports together do a serious disservice to medicine and the health of the public.

Sincerely,

Gregory D. Curfman

Gregory D. Curfman, MD
Executive Editor
New England Journal of Medicine
Boston, Massachusetts

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

RITA F. REDBERG, MD, MSC, FACC
PROFESSOR OF MEDICINE
DIRECTOR, WOMEN'S CARDIOVASCULAR SERVICES
DIVISION OF CARDIOLOGY
EDITOR, ARCHIVES OF INTERNAL MEDICINE

UCSF MEDICAL CENTER, BOX 0124
505 PARNASSUS AVE.
SAN FRANCISCO, CA 94143-0124
(415) 476-6874 FAX (415) 502-7949
EMAIL: REDBERG@MEDICINE.UCSF.EDU

Statement of Rita F. Redberg, MD, MSc.
Subcommittee on Health
House Committee on Energy and Commerce
July 15, 2011

Dear Congressman Waxman,

Thank you for the opportunity to review the Makower Report, which was cited in a recent Congressional hearing on medical devices. I am Rita Redberg, MD, MSc, Professor of Medicine and full time Faculty Member in the Division of Cardiology at the University of California, San Francisco Medical Center. I am Director of our Women's Cardiovascular Service. I am also the chief editor of the *Archives of Internal Medicine*, one of the most preeminent peer-reviewed journals of scientific research in general internal medicine, and have served on the Editorial Board of several other journals. The Archives of Internal Medicine receives over 2500 submissions annually, so I have extensive experience in medical article reviews. Much of my own research has concerned the appropriate and optimal use of medical technology in patient care, and the journal frequently publishes articles related to use of medical devices. My review of this report represents my professional opinion and does not reflect the official position or policy of my institution, or any journal or association with which I am affiliated.

There are several serious methodological issues with the Makower report that render its findings scientifically invalid. Firstly, in order to do a is survey it is essential to have a random sample of a large population, or a high response rate of the target population, otherwise selection bias is present. The Makower report has neither. On page 18, he states that there are "more than 16,000 medical device companies" and of the total, 4, 776 are medical device manufacturers. He surveys a selected group of venture capitalists, and members of the Medical Devices Manufacturers Association. Even in this select group of over 750 medical device companies, the response rate is about 20%. Ironically, Makower states that he is doing this survey to disprove the perception that complaints about the FDA are just from a "vocal minority", but this report seems to be exactly that.

In addition, to the selection bias and unacceptably low response rate, there are additional issues of conflict of interest - present for the authors, funders and survey respondents. All of them are medical device companies or venture capitalists, whose livelihood depends on fast approval of medical devices. It is understandable that their focus and priorities are on rapid approval as time relates directly to costs and their bottom line, but there are other crucial considerations, such as safety and effectiveness of devices to ensure patient benefit. The perspectives of other interested

parties, such as patient groups whose lives are seriously harmed by the approval of unsafe and/or ineffective devices, or physicians who care for such patients, or the FDA are not represented.

Additionally, the report cites a presentation by Ralph Hall, entitled "Using Recall Data to Assess the 510(k) Process" at the Institute of Medicine's July 2010 meeting, to claim that the FDA "does an exceptional job of protecting patients." However, this talk by Professor Hall, who is the CEO of a start-up medical device company and counsels device companies, is not published in any peer-reviewed medical journal and has important inaccuracies. In brief, he argues that the percentage of FDA-approved medical devices, which are recalled by the FDA, is a very small percentage of those that are submitted for FDA approval.[1] However, this analysis uses the incorrect denominator of device submissions – one which is much larger than the correct denominator, the number of devices cleared by the FDA. Only the devices cleared accurately represents the true proportion of devices which can be recalled. The Makower report misses this important distinction by stating that Hall's results were of devices that were "cleared/approved," when, in fact, they were of submitted devices.

Another example to illustrate the inherent bias in the Makower report is with regard to the findings on transparency. He states that 85% of respondents found European Union (EU) processes to be transparent versus just 27% for the FDA. This EU statistic is incongruous with findings of a recent investigation by the British Medical Journal into medical device recalls in the United Kingdom which found that there was no transparency about recalls; the authors were unable to find information about the specific approval process for recalled devices or the risk of harms from those devices from the United Kingdom's Medicines and Healthcare Products Regulatory Agency.[2] They even contacted the manufacturers, but only 2% provided any clinical data. The Notified Bodies, which are responsible for device approval in the EU, refused to provide that information as they stated it was confidential. This peer-reviewed research suggests that the Makower Report's statistic for the EU is inaccurate, likely related to the problems in survey methods and selection bias. What was not addressed in the Makower report that would be helpful in comparing the US and the EU is to include outcomes data – how many patients are benefiting from use of devices, and how many are suffering adverse events and/or recalls. The metric of time to approval is of interest to companies because it directly relates to the cost to the companies of device development, but is of no relevance to patients.

Regarding economics, the Makower Report states that current FDA processes are causing innovators and medical device companies to relocate internationally, sending important tax revenue and jobs away and, therefore, hurting the U.S. economy. However, this argument is faulty because approving unproven and unsafe devices actually hurts the economy by allowing limited healthcare dollars to be spent on expensive devices that do not help patients, which leads to higher health insurance premiums which can lead to economic difficulties and bankruptcies for many small businesses. Technology is the leading correctable cause of rising health care costs. Further, when patients are harmed from unsafe devices, they are unable to work, which presents additional costs. Certainly medical devices have provided important advances to patients, but this evidence of benefit, must be demonstrated, not assumed and studies take time. It would be negligent to use these devices without evidence of benefit in patients, particularly high-risk devices which are often permanently implanted.

The Makower report is helpful in identifying areas that could be improved by the FDA, such as decreased staff turnover. Such turnover, likely related to inadequate funding leads to avoidable and frustrating delays in device review. As FDA Commissioner Hamburg recently stated, "Our

resources are outstripped by our responsibilities…there is a continuing need for expansion of investment."[3] Providing the FDA with more funding and increased resources would likely help to alleviate these difficulties and reduce time to approval without shortchanging the time needed for clinical trials. The calls for consistency in the approval process are important and would help the FDA, as well as the companies.

For all of the limitations above, this study would not be accepted at a peer-reviewed medical journal.

Sincerely,

RITA F. REDBERG, M.D., M.Sc., F.A.C.C., F.A.H.A.
UCSF School of Medicine
Editor, Archives of Internal Medicine
Professor of Medicine
505 Parnassus Ave., Suite M-1180
San Francisco, California 94143-0124
E-MAIL: redberg@medicine.ucsf.edu
PHONE: 415-476-6874
FAX: 415-353 9190

---

[1] Hall R. Using Recall Data to Assess the 510(k) Process. Public Health Effectiveness of the FDA 510(k) Clearance Process: Institute of Medicine, Washington, D.C., July 2010.
[2] Thompson M, Heneghan C, Billingsley M, Cohen D. Medical device recalls and transparency in the UK. BMJ 2011;342:d2973.
[3] Okie S. Reviving the FDA. N Engl J Med 2010;363:1492-1494.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

RITA F. REDBERG, MD, MSC, FACC
PROFESSOR OF MEDICINE
DIRECTOR, WOMEN'S CARDIOVASCULAR SERVICES
DIVISION OF CARDIOLOGY
EDITOR, ARCHIVES OF INTERNAL MEDICINE

UCSF MEDICAL CENTER, BOX 0124
505 PARNASSUS AVE.
SAN FRANCISCO, CA 94143-0124
(415) 476-6874 FAX (415) 502-7949
EMAIL: REDBERG@MEDICINE.UCSF.EDU

Statement of Rita F. Redberg, MD, MSc.
Subcommittee on Health
House Committee on Energy and Commerce
July 17, 2011

Dear Congressman Waxman,

Thank you for the opportunity to review the California Healthcare Institute Report on medical device approvals. I am Rita Redberg, MD, MSc, Professor of Medicine and full time Faculty Member in the Division of Cardiology at the University of California, San Francisco Medical Center. I am Director of our Women's Cardiovascular Service. I am also the chief editor of the *Archives of Internal Medicine*, one of the most preeminent peer-reviewed journals of scientific research in general internal medicine, and have served on the Editorial Board of several other journals. Much of my own research has concerned the appropriate and optimal use of medical technology in patient care, and the journal frequently publishes articles related to use of medical devices. BCG provides professional consulting services to the AMA.
California Healthcare Institute subscribes to the AMA journals via a site license, in addition to the grant. The *Archives of Internal Medicine*, is published by the AMA, but my review of this report represents my individual professional opinion and does not reflect the official position or policy of my institution, or any journal or association with which I am affiliated.

FDA performance should NOT be measured in days to approval, devices are more complex now and require (more) time for a review. This report assumes the faster the FDA approves a device, the better. That may be true from the perspective of a medical device company, but it is not true from the perspective of patients. Patients need to have the assurance that the device they are going to receive has been shown to be of benefit, and that it does not have significant risks. Such studies take time, but are critical so that we can assure patients that their device, often implanted, is a better treatment than not getting the device. Just because a device is new does not mean it is innovative or "cutting-edge", such characteristics must be proven in clinical studies.

It is simply not true that randomized controlled trials (RCT) are not necessary for medical devices, as stated in Sec 2:3. It is absolutely necessary to have a RCT to determine safety and effectiveness for many devices, particularly high-risk devices, which are frequently implanted and not easily removed if it turns out that they have no benefit. RCT can be done for devices, and the most helpful and informative ones have a sham control arm to account for the powerful placebo effect of having a procedure (even an ineffective one). The importance of sham controls was seen in the recent RCT of vertebroplasty[1]. This technology was approved by the FDA and was commonly used to treat osteoporotic vertebral fractures before a randomized controlled trial with sham control was done. However, the RCT showed no benefits to vertebroplasty over sham control, meaning patients were undergoing significant risks of this surgery without any benefit. Clearly, RCT can and should be done, prior to FDA approval, to avoid such

unfortunate situations, which lead to Americans receiving devices with no known benefits and suffering significant device-related adverse events, including death.

It is difficult to evaluate the comparisons (Figure 13) of drug approval times between the European Union (E.U.) and the U.S. as basic data is not provided. The methods do not state what specific drugs were examined, how many drugs were examined, the reasons for delay in the E.U. and U.S., and any statistical analyses performed. Furthermore, there may often be valid reasons for delayed drug approval in the U.S. For example, ticagrelor is a medication which was studied in an international double-blind randomized controlled trial for patients with acute coronary syndrome. Overall results showed that ticagrelor was superior to the current standard of care, clopidogrel, which is a similar medication. However, for the subgroup of patients from the United States, ticagrelor did not show any benefit and, in fact, outcomes were better with clopidogrel.[2] The European Union has approved this medication but the FDA has not yet done so because it is reviewing further information. While on the surface this example would appear to make it seem that the FDA is slower than the E.U. in drug approval, the details show that the FDA is indeed performing its job by diligently investigating if ticagrelor is safe and effective for patients in the U.S. Without examining details for the reasons for delays in drug approval, it is impossible to judge any such differences.

The CHI/BCG report's findings differ from the study published this month in the peer-reviewed journal *Health Affairs* that performed direct drug-drug comparisons for new cancer drugs between the FDA and the European Medicines Agency (EMA).[3] This report found that all drugs approved by both agencies since 2003 were available first to U.S. patients. It found that the mean delay was 138 days and the median delay was 238 days in favor of the FDA. This publication contains information for all of the cancer drugs and their review time by both agencies; it provides data, which can be independently verified, unlike the CHA/BCG report.

Rapid approvals are often done without meaningful clinical data. For example, in 1996, the FDA approved midodrine to treat orthostatic hypotension. This drug was approved based on a surrogate endpoint – one that neither impacted patient morbidity or mortality – with the understanding that the sponsor would conduct adequate post-marketing trials to demonstrate the benefit of this medication. Fifteen years later, despite earning over a quarter billion dollars in sales, the drug's initial sponsor had not conducted the requisite clinical trials. The FDA gave several warnings to the drug company, but to no avail. However, when the FDA attempted to withdraw this medication because there were no clinical trials completed, it faced significant resistance. Therefore, midodrine remains on the market despite no assurances of safety or effectiveness only because the FDA granted accelerated approval fifteen years ago with the promise of clinical trials which never happened.[4]

Similar to drugs, important data re device approvals is not included (figures 14 and 15), such as specific device names, their complexity, the reasons for differences in time to approval, and statistical analyses to check for differences, which again make the validity of the conclusions hard to evaluate. Regardless, rapid approval for high-risk devices is not the highest priority goal. As they are often permanently implanted, it is essential that high-risk devices have adequate assurances of safety and effectiveness prior to approval. A recent report identified five medical devices approved in Europe but not in the FDA which were later found to have safety concerns or a lack of effectiveness.[5] The European Society of Cardiology recently released a consensus document which suggests several reforms for the medical device approval process in Europe because the regulatory framework there was established over 20 years ago and has not kept up with technological advances.[6] The E.U.'s device approval and recall system has been found to lack transparency as there is little publicly available data.[7]

One recent example, which demonstrates the pitfalls of fast approval for high-risk devices without the benefit of clinical data, is the Sprint Fidelis implantable cardioverter-defibrillator. This device was cleared by the FDA via the 510(k) pathway in 2004 without any premarket clinical testing. It was subsequently implanted in 268,000 patients over three years before being voluntarily withdrawn by the manufacturer for lead fractures.[8] Unfortunately, these lead fractures have already led to patient deaths

and having to make difficult choices between repeat risky procedures for lead removal or living with a fractured lead.

Due to the methodological limitations and faulty assumptions described above, it is my opinion that this study would not be accepted in a peer-reviewed medical journal.

There are certainly opportunities to improve efficiency at the FDA and make the agency more transparent. As the CHI/BCG report acknowledges, the scope of the FDA's purview has grown significantly but "federal appropriations have failed to keep up with new mandates." Increased funding and political backing for the agency will help it to perform its tasks better and help ensure that U.S. patients are getting safe and effective drugs and devices.

Sincerely,

RITA F. REDBERG, M.D., M.Sc., F.A.C.C., F.A.H.A.
UCSF School of Medicine
Editor, Archives of Internal Medicine
Professor of Medicine
505 Parnassus Ave., Suite M-1180
San Francisco, California 94143-0124
E-MAIL: redberg@medicine.ucsf.edu
PHONE: 415-476-6874
FAX: 415-353 9190

---

[1] Buchbinder R., Osborne RH., Ebeling, PR., et al.. A Randomized Trial of Vertebroplasty for Painful Osteoporotic Vertebral Fractures. N Engl J Med 2009; 361:557-568 August 6, 2009

[2] Gaglia MA, Waksman R. Overview of the 2010 Food and Drug Administration Cardiovascular and Renal Drugs Advisory Committee Meeting Regarding Ticagrelor. Circulation 2011;123:451.456.

[3] Roberts SA, Allen JD, Sigal EV. Despite Criticism Of The FDA Review Process, New Cancer Drugs Reach Patients Sooner In The United States Than In Europe. Health Affairs 2011;30:1375-1381.

[4] Dhruva SS, Redberg RF. Accelerated Approval and Possible Withdrawal of Midodrine. JAMA 2010;304:2172-2173.

[5] Cohen D, Billingsley M. Europeans are left to their own devices. BMJ 2011;342:d2748.

[6] Fraser AG, Daubert J-C, Van De Werf F, Estes M, Smith SC, Krucoff MW, Vardas PE, Komajda M, et al. Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform. Report of a policy conference of the European Society of Cardiology. Eur Heart J 2011;32:1673-1686.

[7] Thompson M, Heneghan C, Billingsley M, Cohen D. Medical device recalls and transparency in the UK. BMJ 2011;342:d2973.

[8] Hauser RG, Almquist AK. Learning from Our Mistakes? Testing New ICD Technology. N Engl J Med 2008;359:2517-2519.

JAMA & ARCHIVES JOURNALS
American Medical Association

Howard Bauchner, MD
Editor-in-Chief, *JAMA* and Scientific Publications & Multimedia Applications

312 464-2400 Fax 312 464-5520
howard.bauchner@jama-archives.org

SCIENTIFIC PUBLICATIONS & MULTIMEDIA APPLICATIONS
515 North State Street Chicago, IL 60654 USA

July 18, 2011

Representative Henry A. Waxman
Ranking Member, Committee on Energy and Commerce
U.S. House of Representatives
2322A Rayburn House Office Building
Washington, DC 20515

Dear Mr. Waxman:

I write in reply to your request for comments on the report entitled "FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies" by Dr. Josh Makower, Dr. Aabed Meer, and Ms. Lyn Denend. I understand that you have asked several journal editors to review it as they might a submitted manuscript. The topic of medical device regulation by the FDA, including device approval and safety oversight, is of major importance because these products directly affect the health and quality of life of many patients in the United States. Accordingly, there is a need for rigorous research that provides good data to inform the issues of the timeliness and appropriateness of the FDA medical device approval process, and that provides reliable information to compare the efficiency, effectiveness, cost-benefit, and burden of the US and European processes for medical device approval and regulation.

The report by Makower et al is based on a survey of industry executives and was designed to collect information about how the US and European premarket regulatory processes for medical devices compare, about the cost and time involved to navigate the US premarket regulatory processes, and about aspects of the US premarket regulatory processes that are most challenging to innovators. Based on responses from 204 unique companies, the authors report that "survey respondents viewed current US regulatory processes for making products available to patients (the premarket process) as unpredictable and characterized by disruptions and delays" (on page 6 of their report); that the "FDA compared unfavorably to European regulatory authorities" (page 7) in terms of time from companies' first communication about a device to receiving approval to market the device (page 6), as well as in terms of predictability, reasonableness, transparency, and overall experience (page 7); and that the "suboptimal execution of FDA premarket regulatory processes has a significant, measureable cost to US patients in the form of a device lag" (page 7).

The report by Makower at al has several important limitations, including, but not limited to, a selected study population, a low survey participation rate, lack of verification of apparently subjective data, unclear data reporting, and issues surrounding interpretation of the findings for the US and European comparisons. These issues reduce and limit the validity of the reported findings.

First, it appears that those who responded to the survey were from a select group, selected based on invitations to participate limited to companies in the MDMA, NVCA, and medical technology state associations. The study does not provide sufficient information to judge whether this small sample is representative of US medical technology companies. In addition, the survey response rate is low, increasing the likelihood of selection bias, particularly if the invitation to participate indicated the reason for the survey; in that case, respondents may have been more likely to participate if they were dissatisfied or had negative experiences with the FDA process.

Second, the study report does not include the survey instrument or details about survey development and validation, so it is not possible to determine whether the questions were formed in a neutral way, or whether their wording or ordering may have created leading questions or a biased response. Based on the results, it appears the questions were designed to assess respondents' impressions, and opinions, and other subjective measures. There does not appear to have been any attempt to assess the accuracy of these subjective responses, for example, by requesting data through correspondence or internal documents, or by auditing a subset of companies and obtaining objective corroborating data.

In addition, it is unclear whether the responses were based on a respondent's overall opinion of the process at FDA or a company's single recent experience. It also appears that different participants received different surveys and that some companies provided more than one response to some items. However, the authors do not provide information about the number who did so, which questions these responses addressed, whether these multiple responses were aggregated with others, or whether there was clustering by company. Moreover, it is not clear whether all respondents had experience with both the US and European systems, or whether in some cases the comparisons were made between responses of subsets of individuals who did not respond to both sets of questions.

Third, there are several issues with interpretations related to the comparisons of the US and European regulatory processes. The authors interpret FDA approval time lines as being long, but without any background information or benchmark as to what constitutes appropriate time frames; the comparison with EU does not necessarily provide a benchmark of appropriateness, only of an alternate process. Throughout the report, the authors indicate that the delay in approval and availability of devices compared to the EU has resulted in worse care being available for US residents. However, the authors do not provide any evidence that this delay or lack of availability leads to adverse health outcomes. In addition, the authors do not provide data indicating that the EU system is comparable to the US system with the exception of the approval process/time frame. There may be other factors that mitigate the effects of a shorter time frame in the EU, and there may be other differences with respect to the regulatory system and environment between the US and EU that have not been assessed.

Even though the authors have acknowledged several of these important study limitations (page 19 of their report), such acknowledgement does not mitigate the threats to validity created by these methodological issues. Given the extent of these limitations, the inferences and conclusions that can be reliably drawn from this report are limited. When the findings of a statistical survey and report cannot be considered definitive, they may be viewed, at best, as hypothesis generating, perhaps leading to a more thorough exploration in more rigorously designed future studies.

Sincerely,

Howard Bauchner, MD
Editor in Chief, *JAMA* and Scientific Publications

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

The Honorable Henry A. Waxman
House of Representatives
Washington, D.C. 20515-0530

JUL 18 2011

Dear Mr. Waxman:

Thank you for your request for the Food and Drug Administration's (FDA or the Agency) comments on two industry-sponsored studies regarding FDA's performance on the review and approval of medical devices. Over the past few months a number of reports have been issued by or supported by the medical device industry regarding the Agency's performance on the review and approval of medical devices, especially as compared to that of the European Union (EU). Many of these studies employ questionable methodologies and report data that differs significantly from that which is collected as part of FDA's obligations under the Medical Device User Fee Act (MDUFA).

You asked for FDA's comments on the November 2010 report entitled "FDA Impact on US Medical Technology Innovation" by Josh Makower, MD, Consulting Professor of Medicine, Stanford University and CEO, ExploraMed Development, LLC, which was also supported by the Medical Device Manufacturers Association (MDMA) and the National Venture Capital Association (NVCA) (Makower Survey); and the February 2011 Report entitled "Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry," by the California Healthcare Institute and the Boston Consulting Group (CHI/BCG Survey).

We have restated your questions in bold, followed by our responses.

Makower Survey

1. **What are the major methodological issues (whether positive or negative) of this study?**

Of the more than 1,000 companies asked to complete the survey, only 204 responded. For some of the individual survey questions, fewer than 100 companies responded. Therefore, the response rate for the survey overall is 20.4 percent, and for some of the questions it is less than 10 percent. These reporting rates are likely to produce an inherently biased result because they are not based on a representative sample of all medical device companies. In fact, research has shown that the persons most likely to respond to a survey are those who are dissatisfied. It is also important to note that PwC (formerly PricewaterhouseCoopers LLP), which was retained to ensure quality control of the survey, did not assess the study methodology.

In addition, the claim that survey respondents include "approximately 20 percent of all public and venture-backed medical device manufacturers in the U.S. that are focused on

bringing innovative new technologies to market to improve the public health" is a gross overstatement. The authors note that 90 percent of the companies that responded were privately-held, venture-backed companies with a median of 33 employees. The remaining 10 percent of respondents (i.e., 20 companies) do not make up 20 percent of all public medical device firms in the United States. In fact, the study was not sent to the majority of U.S. medical device manufacturers. Instead, the survey was sent primarily to "small, early-stage entities, focused on a single product family," who had limited experience with the FDA review process, which is reflected by the fact that only 55 percent of survey respondents had completed a traditional premarket notification (510(k)) and only 32 percent had gone through the premarket approval (PMA) process. These numbers indicate that some respondents had never gone through the process of getting a product reviewed by the FDA.

2. Please comment on the response rate for the survey overall, and for the time to first contact subgroup.

As noted in response to Question 1 above, the response rate for the survey overall is 20.4 percent, and for some of the questions it is less than 10 percent. For the time to first contact subgroup, only 15 respondents answered the questions with regard to a 510(k) submission. The authors do not give the response rate for the data they report regarding PMAs, but since only 32 percent of all respondents had gone through the PMA process, if the authors had a 100 percent response rate to these questions (which is unlikely given that they admit that some questions had an overall response rate of less than 10 percent), the maximum number of respondents would be 65.

3. Please discuss the methodology used in the study to compare EU and U.S. approval times.

The authors note that "the earliest interaction between company and regulatory body was used as the starting point for evaluating U.S. and European review timelines relative to one another." However, communications between FDA and a sponsor occur far earlier in the device development pathway, when clinical data is required, than they do in the EU, generally before an Investigational Device Exemption (IDE) is submitted to FDA for approval. Therefore, this is an "apples to oranges" comparison that will show an artificial disparity in review times.

Devices submitted to FDA under a PMA are high-risk devices. These devices generally require data from a pivotal clinical trial to demonstrate safety and effectiveness to support their marketing applications, unlike in the EU. Sponsors most often begin interacting with FDA before they even begin designing their clinical trials so as to ensure that the clinical trials are designed to yield scientifically valid and useful results. These interactions are critical to a successful device approval. By contrast, in the EU, sponsors typically meet with a Notified Body (a private company) before or around the time of submitting a premarket application. The difference in starting points for communications between the United States and the EU can be years. The same circumstances apply for 510(k)s that require clinical data, where sponsors may meet with FDA prior to submitting

an IDE. Regardless, sponsors will communicate with FDA by the time they submit their IDE. As such, the statement that "American patients have to wait on average a full two years longer than their European counterparts for many life-saving and life-enhancing technologies" is misleading.

CHI/BCG Survey

1. What are the major methodological issues (whether positive or negative) of this study?

The study uses the wrong data set to measure the time to a decision. The data expressed in the CHI report are based on clearance or approval decisions for 510(k)s and PMAs made during each year (decision cohort). While sometimes informative, using decision cohorts is contrary to how FDA has been reporting its performance on MDUFA goals to Congress for almost a decade. The difference has to do with decision cohorts (the year in which a decision is made) versus receipt cohorts (the year in which a submission is received). Receipt cohorts are generally more informative about performance because most of the work on an application occurs in its year of receipt. On the other hand, if FDA makes good progress on older applications by making decisions on them in a given year, what might otherwise be improved performance would be reflected as a longer review time for that year if a decision cohort is used.

For example, a PMA application may be received by the Agency in 2006, but a decision on that submission may not occur until 2008. When using decision cohorts to assess FDA's performance on this PMA, it would be included in the performance data for 2008, rather than being compared to how FDA performed on all other PMAs received in 2006. Performance metrics based on decision cohorts compare applications that were received in many different years; therefore, there is no baseline upon which to make a comparison.

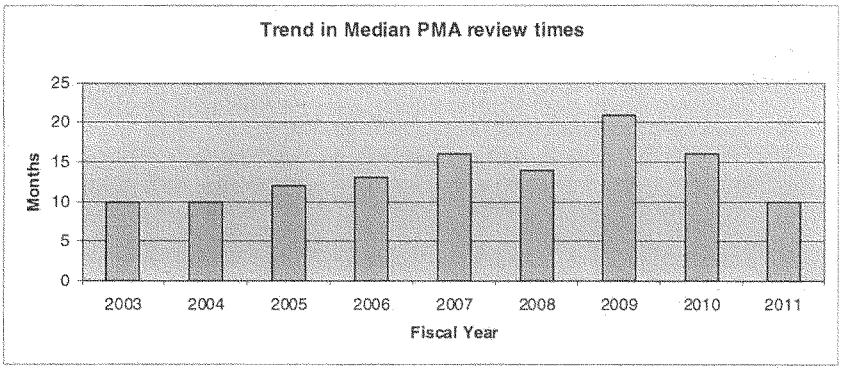
When FDA tracks its performance, we use receipt cohorts so that we know how we performed on applications we received in each year and we can identify the outliers. We also can track other performance trends by keeping track of how we review applications we received in a given year, because that metric allows us to gauge our work during the time we were actively reviewing an application. We can see how much time we took to review an application as compared to how much time industry took to respond to requests for information. We can also better assess the impact of reviewer attrition rates during those years, overall submission volume, and other factors on review times. Using decision cohorts, as is done in the CHI/BCG survey, eliminates these subtleties from the data and paints a less meaningful picture of the Agency's review performance.

2. Please comment on the time to decision data presented in the study.

As discussed above, the CHI/BCG survey notes that "complex PMA submittals saw review periods increase 75 percent over the MDUFMA I (2003-2007) average to 27 months in 2010." However, over the past nine years, the average (mean) time to reach a

decision on an original PMA has varied. The number of PMAs FDA receives each year is relatively small. Therefore, the mean review time can be significantly affected by one or two outliers. Thus, it is most appropriate to use the median time (middle value) to a decision when looking at trends in PMA data to eliminate the effect of outliers. However, the CHI/BCG survey uses the mean time to a decision, which can be skewed by one or two outlier submissions.

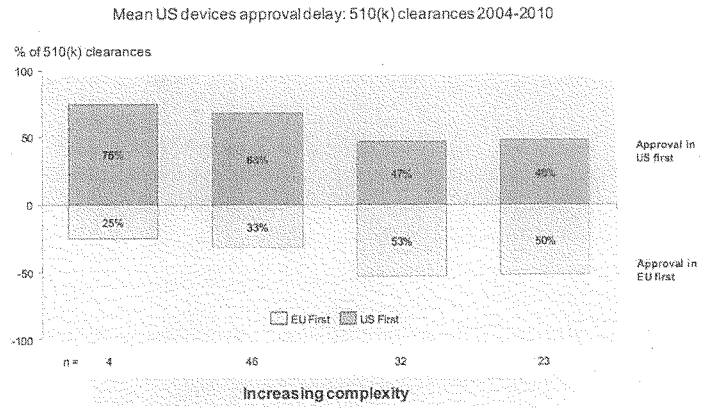
As is shown in the chart below, if the data used by CHI is presented using the median time to a decision (total time) rather than the mean time, it reflects that time to decision for PMAs in 2010 is not going up but rather is less than 2009 and closer to our performance in 2007.



The CHI/BCG survey also notes that "[f]or 510(k) submissions, the approval time has increased 43 percent to an average of 4.5 months in fiscal year 2010 over the average of about three months under the MDUFMA I years of 2003-2007." While the percentage may sound high, the increase in total time to a decision is about six weeks. The increase in time to a decision described by the study is predominantly due to increases in the time it takes industry to provide the information necessary for FDA to make a decision. There are several reasons for this increase, including poor quality submissions from sponsors and FDA asking inappropriate questions.

3. Please discuss the methodology used in the study to compare EU and U.S. approval times.

The CHI/BCG survey claims that there is a clear trend that the more complex, and often cutting edge, a product is, the more likely it is to be approved first in Europe versus the United States. However, based on the following chart from the study, it is clear that 510(k)s without clinical data, which is about 90 percent of the 510(k)s we review and about 80 percent of the devices we review premarket, come on the market in the United States first as often or more often than in the EU.



Note: Represents original 510(k) applications without clinical data. Devices classified using EU standard I-IIa-IIb-III where classification I is least risky while Class III is most risky
Source: Data collected from 16 different medical device companies, where total sample size n = 205 data based on 105 devices for which EU classification was available

For more than a decade, Europe has often approved high-risk devices that would be subject to PMA applications in the United States more quickly for one simple reason: FDA, by law, requires that devices be both safe and effective. That is, devices must provide clinical benefit to American patients. Europe requires only that the device be safe and fit for its intended use with no requirement to demonstrate benefit. As discussed in response to this question regarding the Makower survey, comparing review times for the United States and EU is an "apples to oranges" comparison that does not take into account the difference in the review standards between the two regulatory regimes.

Makower Survey and CHI/BCG Survey

1. Are there issues not addressed at all in either study that might be helpful in a comparison of the EU and U.S.?

As discussed above, neither the Makower survey nor the CHI/BCG survey account for the significant differences in the regulatory requirements of the United States versus EU systems. These differences include:

- In the EU, manufacturers do not have to demonstrate that their products are effective at treating or diagnosing the disease or condition for which they are approved;

- In the EU, manufacturers pick and pay for private companies, of which there are over 70, to review and approve devices by giving them a CE mark. These decisions are kept confidential and are not released to the public or EU regulatory bodies. These private companies, called Notified Bodies, are each

certified by any one of the 27 member countries of the EU, but the decision to approve a device by one Notified Body applies to the entire EU. There has been near unanimous agreement in the EU that the oversight of Notified Bodies is inadequate and in need of significant improvement; and

- In the EU, there is little to no publicly accessible, centralized system for collecting and monitoring information about device approvals or safety problems.

Furthermore, comparisons between the U.S. and EU systems are challenging because the European device review process is less transparent than FDA's, due to the absence of publicly available information about device approvals and safety problems.

The difficulty in making robust comparisons has recently been highlighted by several prestigious European medical journals. These journals have noted that it is nearly impossible to assess the public health impact of the lack of an efficacy requirement, because there is no centralized source of data in the EU. Notified Bodies are not required to make their conformity decisions public and there is not a main database of recall information. There is anecdotal evidence that products reach the EU market that are later shown to be unsafe or ineffective, often when they are undergoing pivotal clinical trials to support U.S. approval.

The European Society of Cardiology (ESC) recently issued a "case for reform" of the European medical device regulatory system and their recommendations included creating a unified system, stronger clinical data requirements, and more accountability for notified bodies.[1] The ESC cites examples of many different cardiovascular technologies that were implanted in patients in the EU that were then proven to be unsafe and/or ineffective through clinical trials required under the U.S. system and removed from the European market. A recent article in the British Medical Journal discusses the opacity of the European medical device regulatory system, with regard to access to decisions regarding device clearances.[2] The article cites the FDA system's transparency as helping physicians to make informed decisions on which devices to use and giving patients access to information on devices that will be used on them.

In 2010, the clinical director of the UK's regulatory body overseeing devices said "I'm appalled at how many devices are brought to market with a lack of appropriate clinical data. ... A lot of devices have given me cause for concern because of the lack of adequate clinical evidence...."[3] She went on to point out that many Notified Bodies do not know how to adequately assess, or challenge, clinical data. "These are commercial

---

[1] See "Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform," Fraser, et al., *European Heart Journal*, May 2011.
[2] See "Medical-device recalls in the UK and the device-regulation process: retrospective review of safety notices and alerts," Heneghan, et al., *British Medical Journal*, May 2011.
[3] See "EU must tackle clinical trial shortfalls as current lack of evidence is 'appalling'. Maxwell, Amanda, *Clinica*, July 2010.

organizations, many of whom are reluctant to challenge because they fear losing their clients and for their survival."

Based upon identified weaknesses of the EU system, the European Commission has undertaken a review of its device regulatory system. As the Commission stated in 2008, "Experience indicates that the current system does not always offer a uniform level of protection of public health in the European Union. New and emerging technologies have challenged the current framework, highlighting gaps and pointing to a certain scarcity of expertise .... And finally, the legal system has been criticized as being too fragmented and difficult to follow and fraught with national variation."[4] Additionally, a report released by the Belgian Health Care Knowledge Centre[5] calls upon the European Commission to implement reforms to make the EU review process for high-risk devices more like that of the United States.

Thank you again for your interest in this matter. If we can be of further assistance, please let us know.

Sincerely,

Michael Mittal

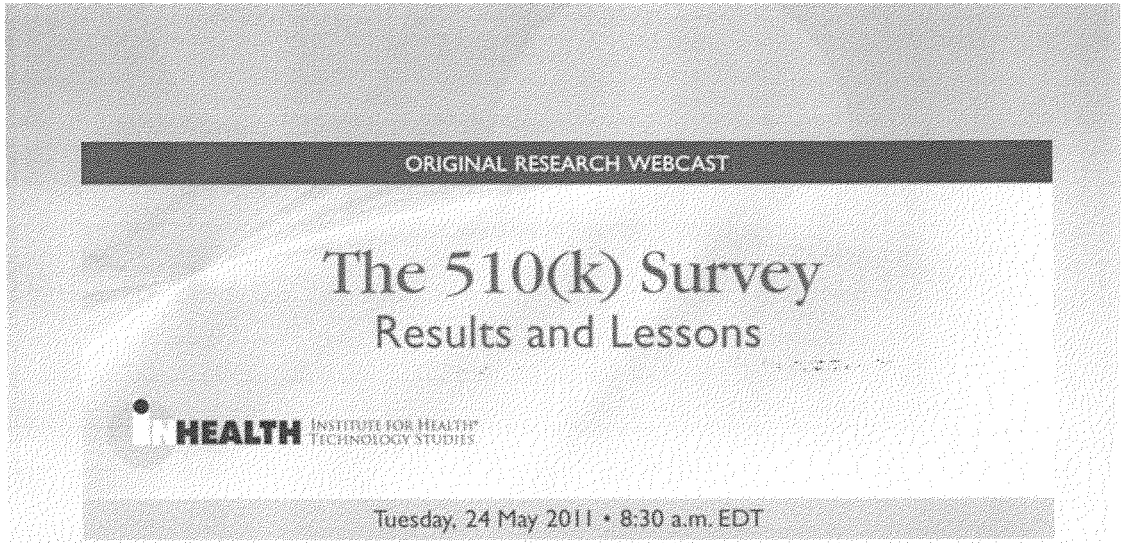
for Jeanne Ireland
Assistant Commissioner
for Legislation

[4] See "Recast of the Medical Devices Directives: Summary of Response to the Public Consultation," European Commission, December 2008.
[5] See "The pre-market clinical evaluation of innovative high-risk medical devices," KCE reports 158C, Belgian Health Care Knowledge Centre, 2011.

Mr. STEARNS. Mr. Terry wanted to put this New York Times article in, the "Medical Treatment, Out of Reach." So ordered.

Then I have a 510(k) survey results researchers from Northwestern University into the record. The Northwestern researchers surveyed more than 350 medical device development specialists on their experience with FDA and medical device review process compared with that of the European Union, and they show that two-thirds of the small medical device and diagnostic companies are obtaining for new products in Europe first and the survey shows that 76 percent of the respondents said preparation requirements for 510(k) submission were uncertain or unclear, and I think this is a good study to be part of the record, and FDA needs to provide predictability and certainty for companies or they will continue to go to Europe. With that unanimous consent, so ordered.

[The information follows:]

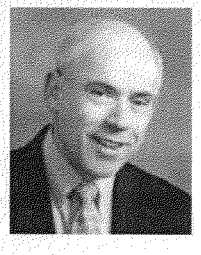

ORIGINAL RESEARCH WEBCAST
The 510(k) Survey
Results and Lessons
iHEALTH INSTITUTE FOR HEALTH® TECHNOLOGY STUDIES
Tuesday, 24 May 2011 • 8:30 a.m. EDT

ORIGINAL RESEARCH WEBCAST

The 510(k) Survey
Results and Lessons

HEALTH INSTITUTE FOR HEALTH TECHNOLOGY STUDIES

Tuesday, 24 May 2011 • 8:30 a.m. EDT



Moderator

Robert J. Rubin, MD
Clinical Professor of Medicine, Georgetown University
Member, InHealth Board of Directors
Chair, InHealth Research Council

Presenting Investigators

John H. Linehan, PhD
Professor of Biomedical Engineering
Northwestern University

Jan B. Pietzsch, PhD
President and CEO, Wing Tech Inc.
Consulting Associate Professor of Management Science and Engineering
Stanford University

iHEALTH INSTITUTE FOR HEALTH TECHNOLOGY STUDIES

A Comprehensive Analysis of the FDA 510(k) Process

Industry Practice and the Implications for Reform

John H. Linehan, Ph.D. *Northwestern University*

Jan B. Pietzsch, Ph.D. *Wing Tech Inc.; Stanford University*

National Press Club, Washington, D.C.

May 24, 2011

- Revised July 19, 2011 -

NORTHWESTERN
UNIVERSITY

NORTHWESTERN UNIVERSITY

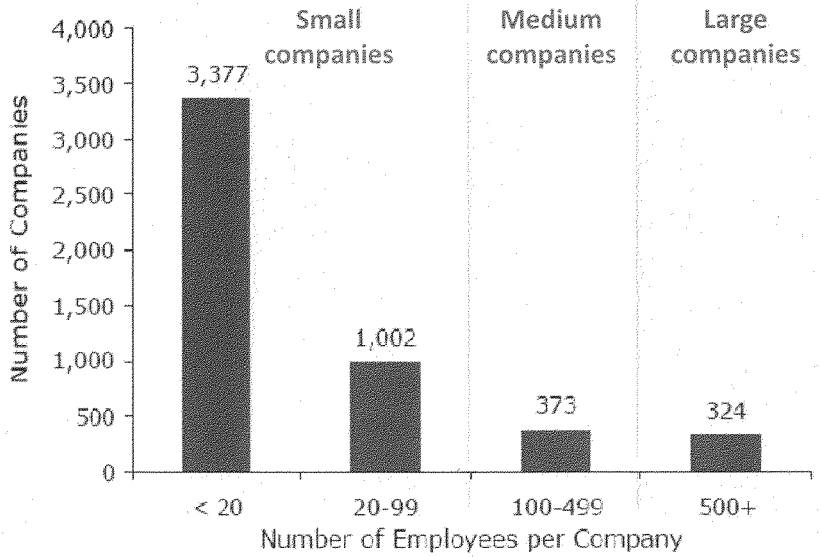
Outline

- The Medical Device Industry and Device Development
- Introduction to the Research Study
  - Objectives and Methodology
  - Respondent Characteristics
- Key Findings
  - Predictability and Interaction with FDA
  - Different Impact on Large and Small Companies
  - International Comparison
- Observations: Opportunities for Improvement
- Concluding Remarks

The Medical Device Industry and Medical Device Development

NORTHWESTERN UNIVERSITY

Medical Device Companies by Size

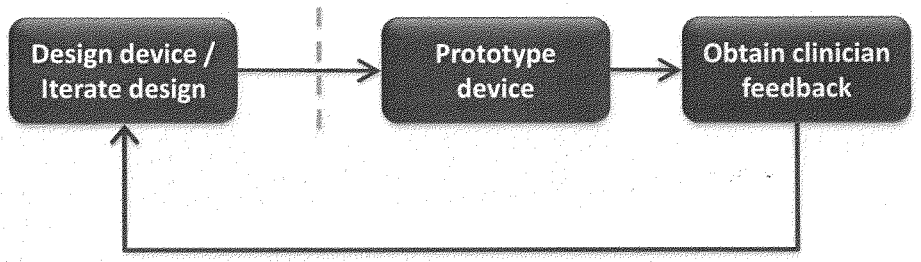


% of Total US Medical Device Employment	28%	18%	54%

Source: Number of companies: US Dept of Commerce, 2001. Employment: US Census, 2008.

NORTHWESTERN UNIVERSITY

Device Development Is an Iterative Process



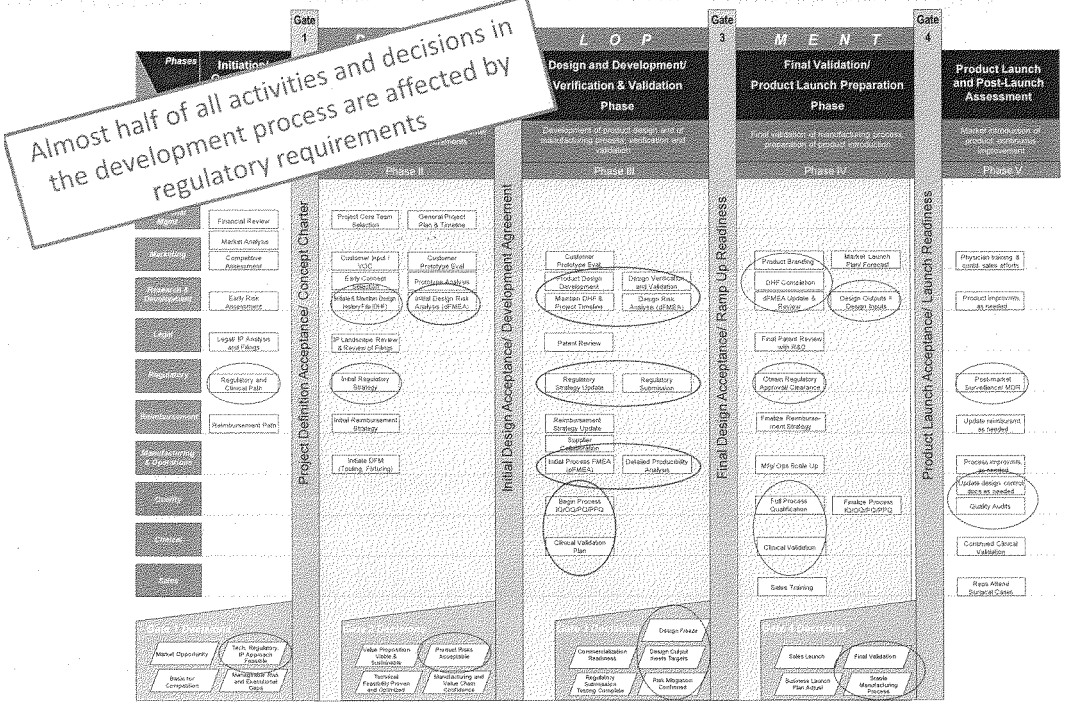
- Medical device development is a highly iterative process.
- Need to improve product continuously through frequent, positive iterations, while avoiding unnecessary iterations
- Efficient planning and execution requires predictable process.

NORTHWESTERN UNIVERSITY

Medical Device Development Functions

- Cross-Functional Management
- Marketing
- Research & Development
- Legal
- Regulatory
- Reimbursement
- Manufacturing & Operations
- Quality
- Clinical
- Sales

Impacts of Regulation on Device Development



Introduction to the Research Study

NORTHWESTERN UNIVERSITY

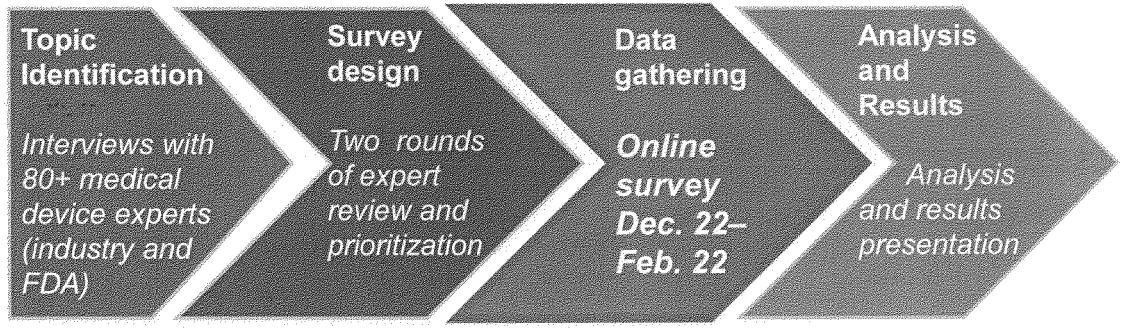
Study Objective and Methodology

- Elicit from those engaged in medical device development, what seems to work well and how the 510(k) regulatory process could be further strengthened.

- Collect comprehensive data set to provide the basis for constructive input to strengthening the process:
  - Timelines
  - Interactions with the agency
  - Issues and challenges in current implementation
  - Comparison among international regulatory programs

NORTHWESTERN UNIVERSITY

Approach and Study Methodology



8/2010 5/2011

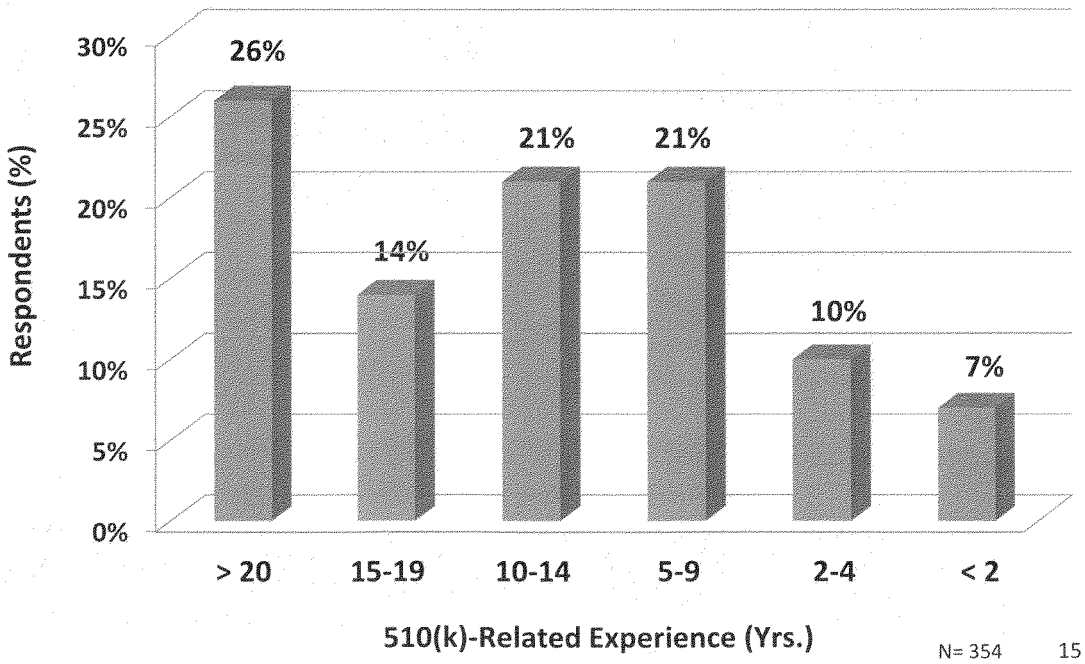
NORTHWESTERN UNIVERSITY

Approach and Study Methodology

- Target respondents:
  - Individuals closely involved with the 510(k) process
  - Broad outreach through professional societies, industry groups, and trade media
- Survey Structure:
  - General part and device-specific part
  - 86 questions total
- Responses:
  - N=356 respondents total
  - Number of respondents varied per question, as not all questions were answered by every respondent
  - N per question stated for each question in graphs and appendix

NORTHWESTERN UNIVERSITY

Respondents' 510(k)-Related Experience



N= 354

15

NORTHWESTERN UNIVERSITY

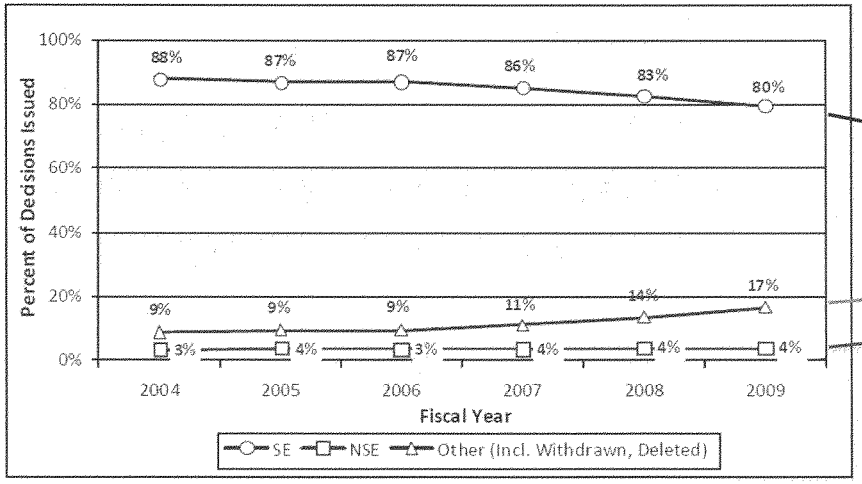
Representativeness: Breakdown by Device Type

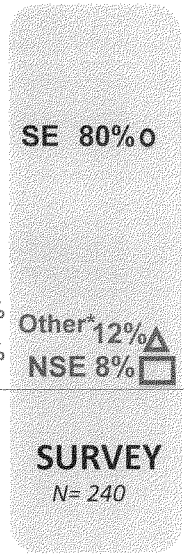
Type of Device	Actual % of FDA Applications	Survey Respondents %
Surgical, Orthopedic, and Restorative Devices	28%	37%
Cardiovascular Devices	13%	23%
Anesthesiology, General Hospital, Infection Control,and Dental Devices	23%	13%
Reproductive, Abdominal, and Radiological Devices	17%	7%
Ophthalmic, Neurological, and ENT Devices	6%	5%
Chemistry and Toxicology Devices	5%	3%
Immunology and Hematology Devices	3%	2%
Microbiology Devices	2%	1%
Other	3%	9%

Actual % FDA applications: Based on all applications to FDA in 2008-2010 (See FDA database at www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.
Survey Respondents %: Based on respondent's statement about device field with most extensive 510(k) experience.

FDA's Internal Assessment compared to Survey Responses

Figure 4.9. 510(k) Decisions Issued: FY 2004-2009





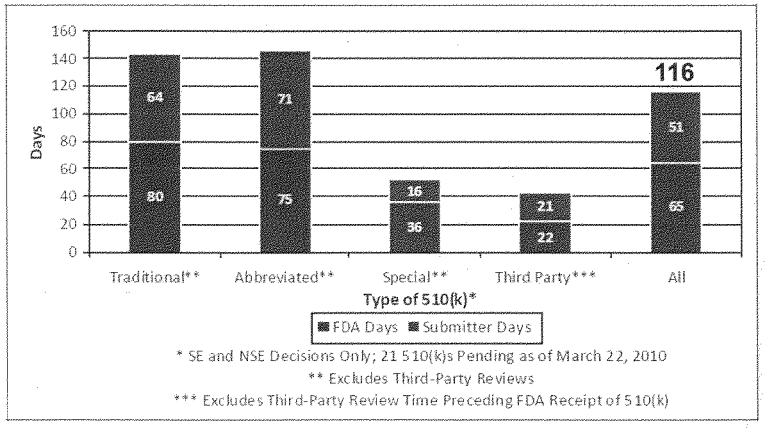
Source: - FDA CDRH, 510(k) Working Group - Preliminary Report and Recommendations, Vol. 1, August 2010.
- MDUFA Meeting Report, 2011.

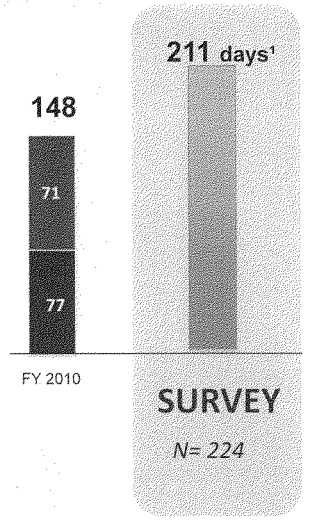
* Includes the following responses: De-Novo, Converted to PMA, Other

NORTHWESTERN UNIVERSITY

FDA's Internal Assessment compared to Survey Responses

Figure 4.5. Average Time to 510(k) Decision by Type of 510(k): FY 2008 Receipt Cohort [80]



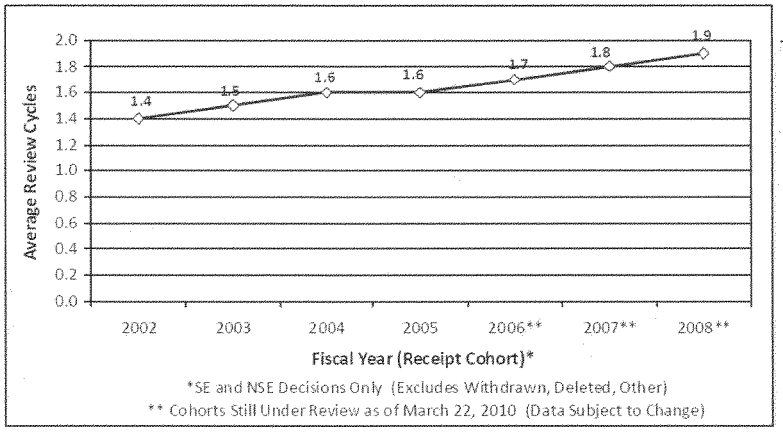


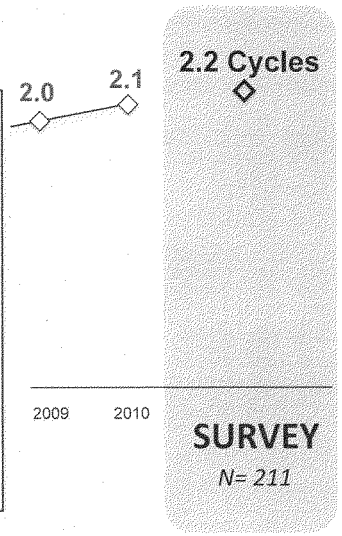
Source: - FDA CDRH, 510(k) Working Group - Preliminary Report and Recommendations, Vol. 1, August 2010.
- MDUFA Meeting Report, 2011 *(as amended/corrected by FDA 7/2011)*

[1] SE and NSE only.
Avg. duration for SE: 204 days (N=179); NSE: 279 days (N=18); Withdrawn: 330 days (N=13), with long tail.

FDA's Internal Assessment compared to Survey Responses

Figure 4.8. Number of 510(k) Review Cycles: FY 2002-2008



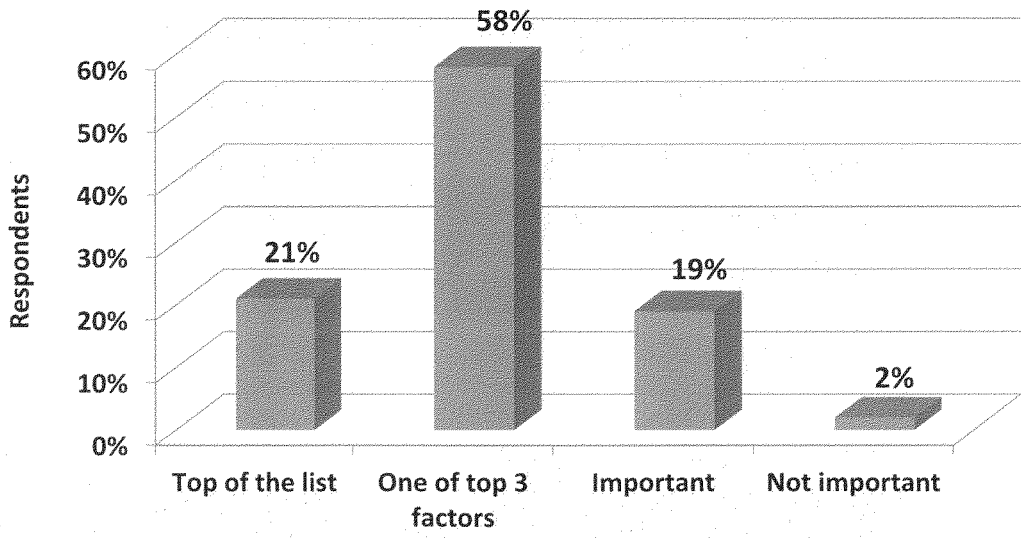


Source: - FDA CDRH, 510(k) Working Group - Preliminary Report and Recommendations, Vol. 1, August 2010.
- MDUFA Meeting Report, 2011.

N= 211; SE: 2.1 cycles (N=191); NSE: 2.8 cycles (N=20)
Withdrawals (not included in computation): 2.9 cycles (N=14)

Key Findings
Predictability and Interaction with FDA

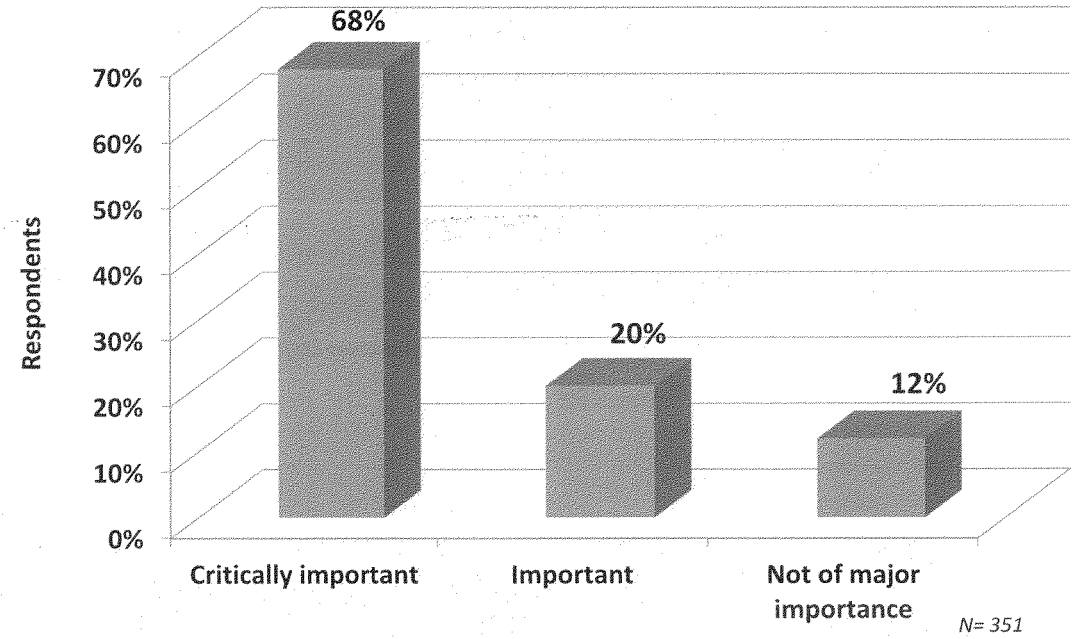
Importance of Regulatory Requirements in Decision to Invest in a New Product



N= 351

How important are regulatory requirements to your business decision to a major investment in a new product?

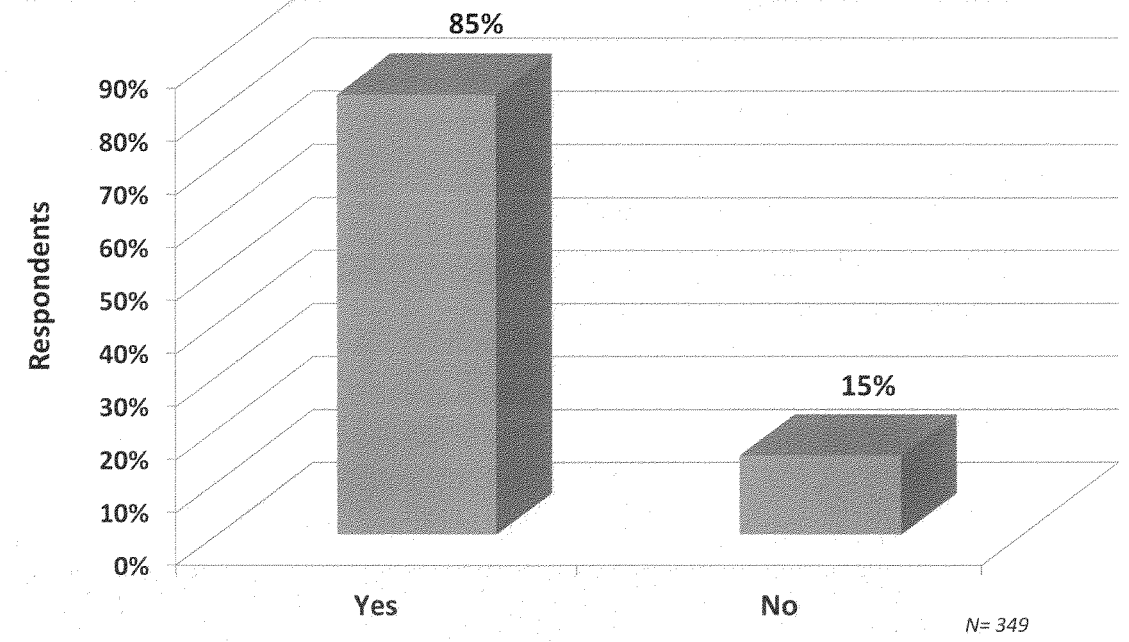
Importance of Regulatory Process Predictability for Decision about First Country for Market Launch



For the technologies you have worked on, how important is predictability of the regulatory process in deciding first country for market launch?

NORTHWESTERN UNIVERSITY

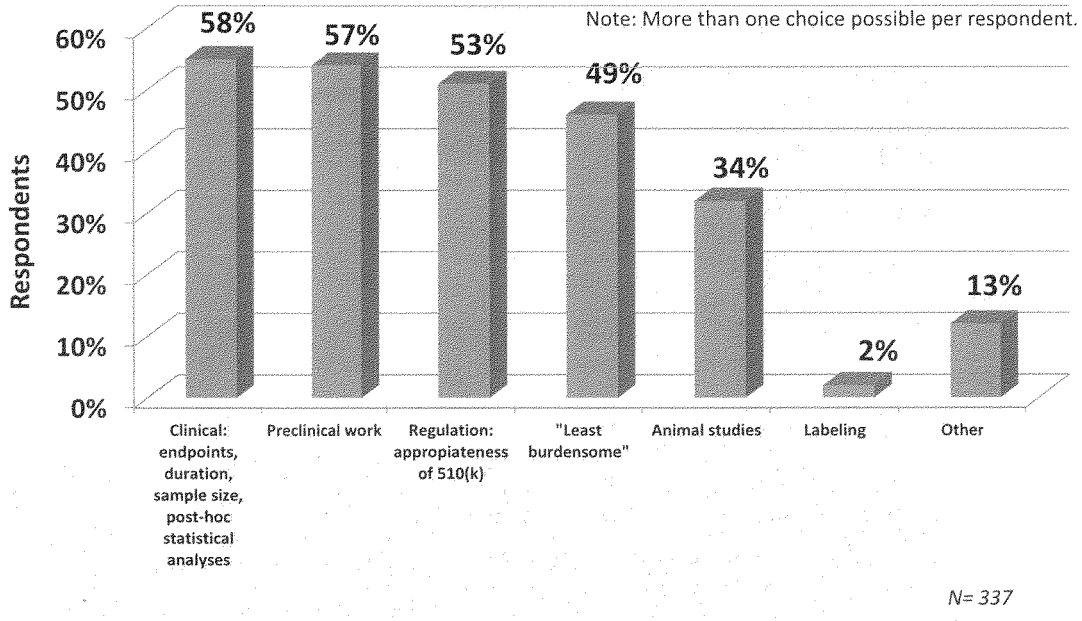
Respondents Perceiving Substantive Changes in FDA Review Process



From your experience in the last 3 years, have you perceived any substantive changes in the FDA review process and/or clearance decision of a 510(k) submission?

NORTHWESTERN UNIVERSITY

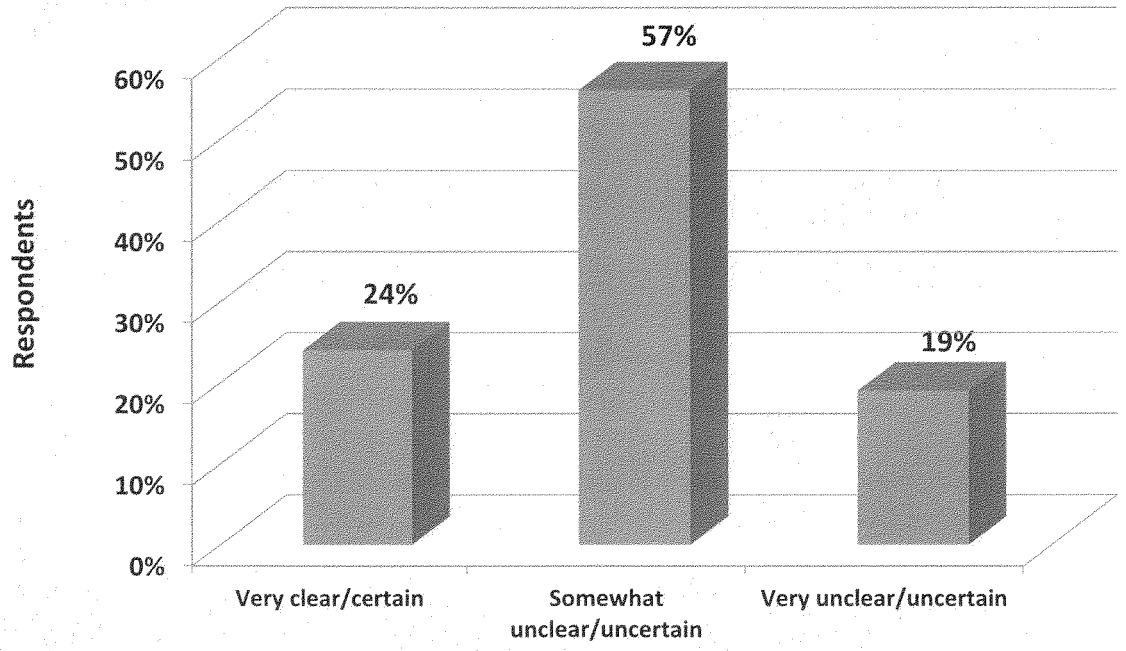
Perceived Changes in FDA's Requirements



In the last 3 years, in what specific areas have you perceived changes in the FDA's requirements?

NORTHWESTERN UNIVERSITY

Clarity of Preparation Requirements for a 510(k) Submission

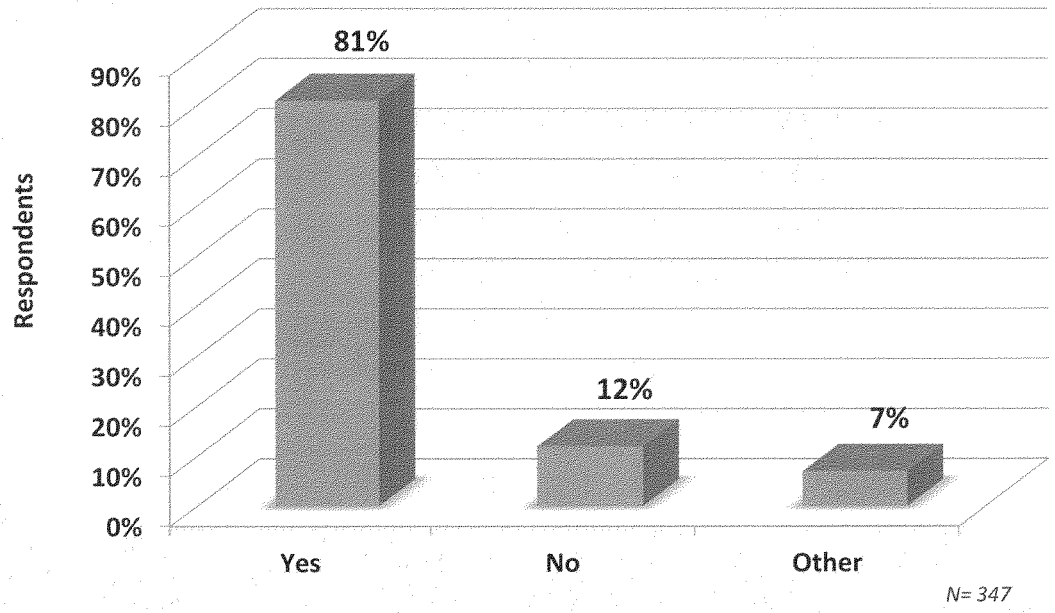


N= 354

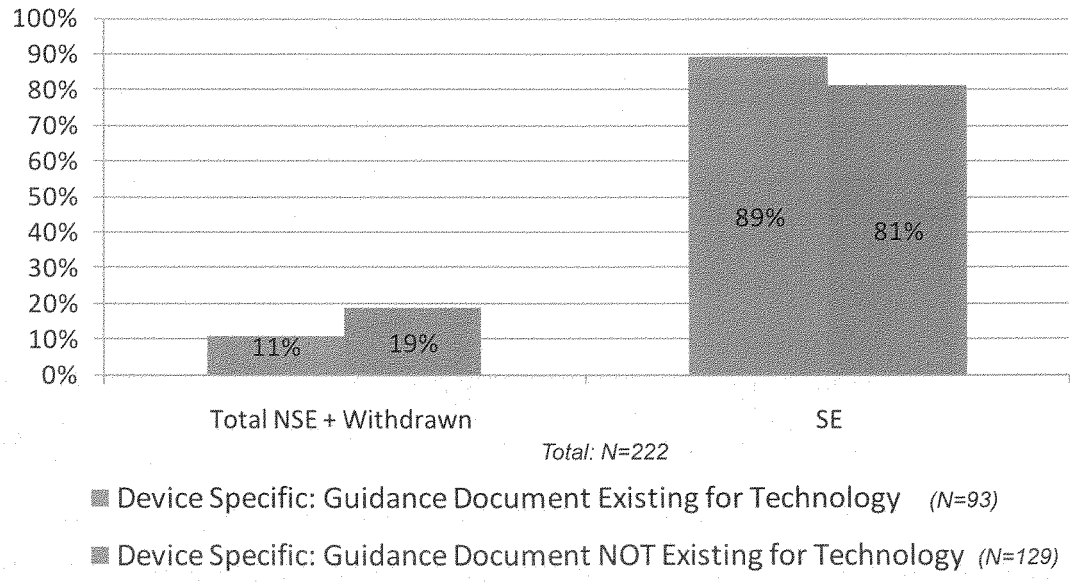
Based on your understanding, what is the current level of clarity of the requirements for preparation and submission of a 510(k)?

NORTHWESTERN UNIVERSITY

Have Guidance Documents been Critical to your Company in Preparing Successful Submissions?

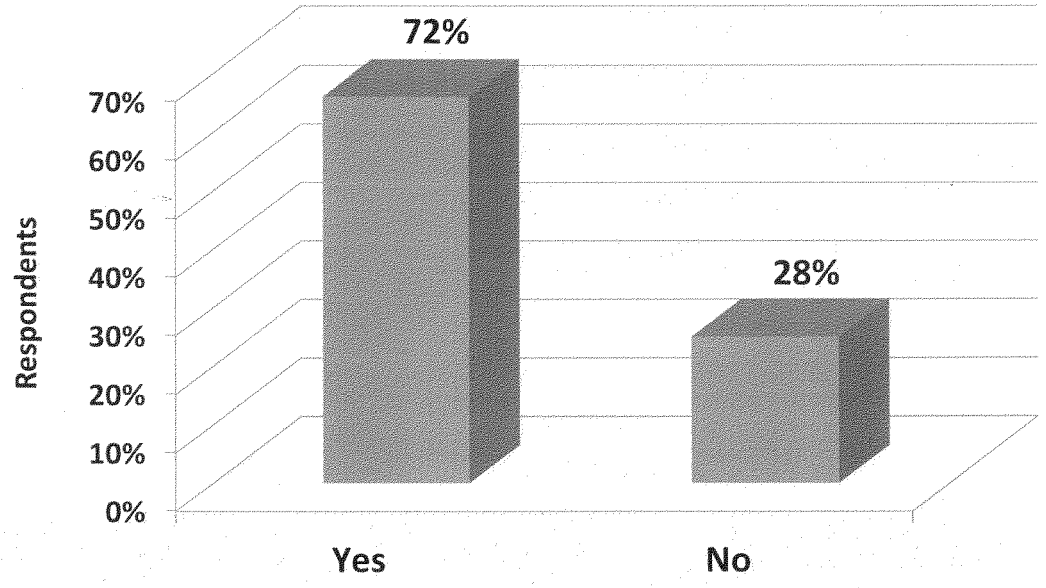


Availability of Guidance Document has an Impact on the Ultimate Decision



NORTHWESTERN UNIVERSITY

Respondents Perceiving Differences Between Guidance Document and FDA Review

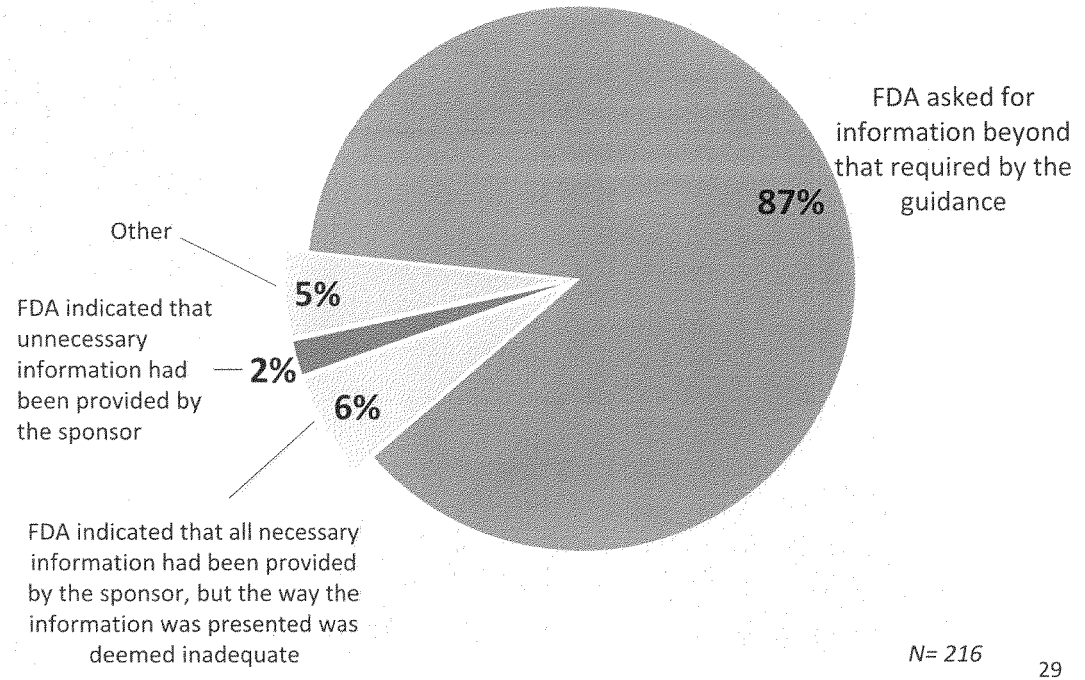


N= 300

If an appropriate guidance existed and was used by your company during submission of a 510(k), did you perceive any difference between the guidance document and the way the FDA reviewed your submission?

NORTHWESTERN UNIVERSITY

Reason for Perceived Difference between Guidance Document and FDA Review

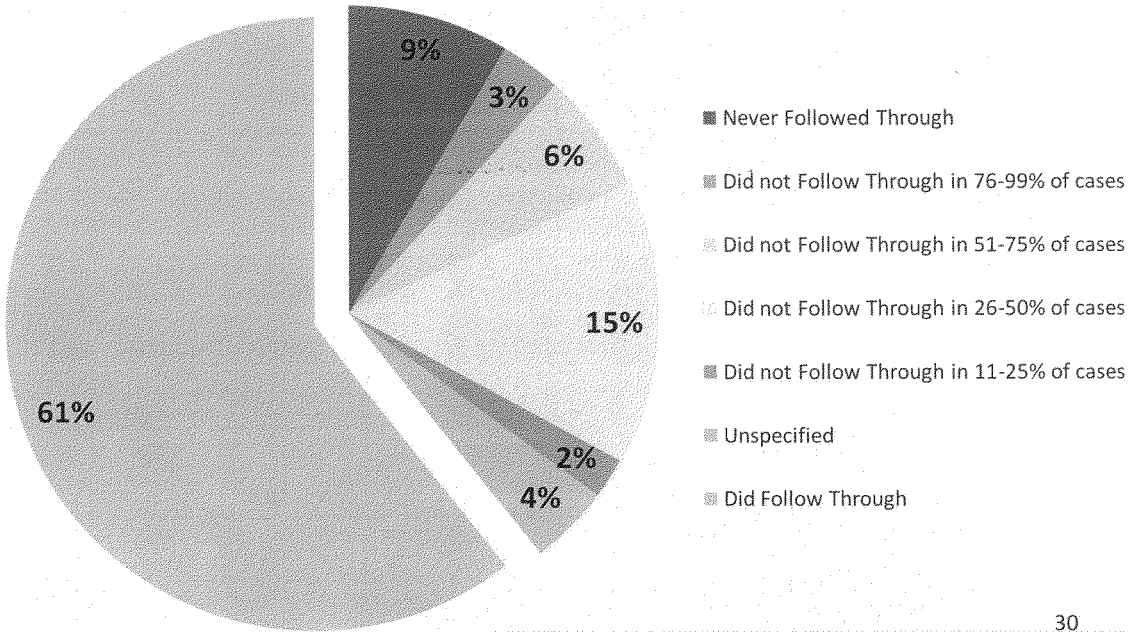


N= 216

NORTHWESTERN UNIVERSITY

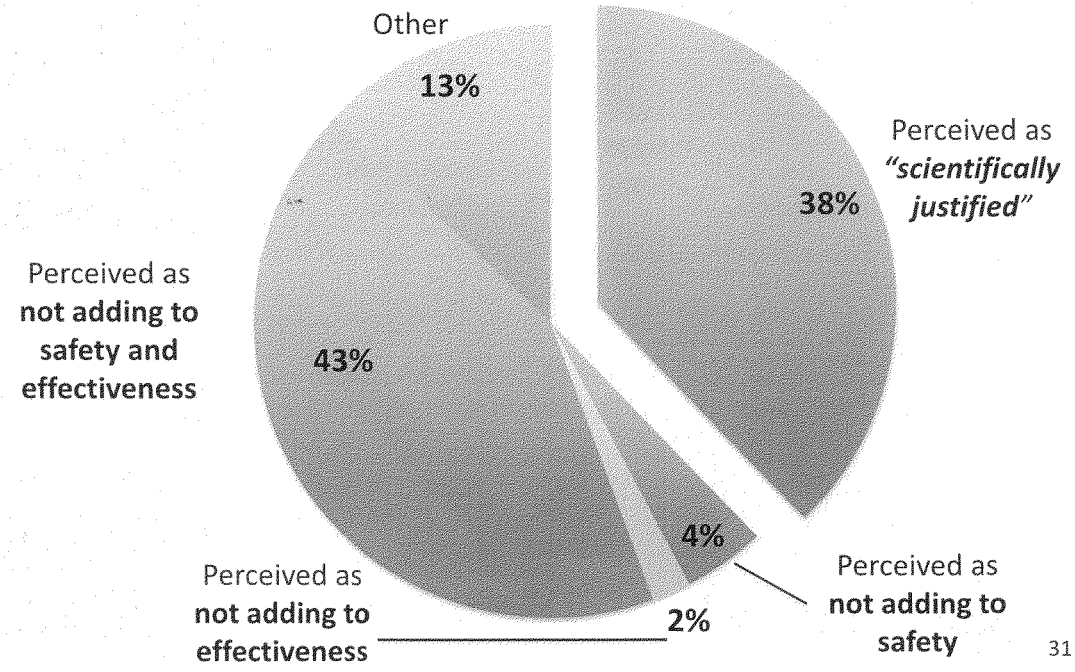
Perceived Difference between Pre-Submission Meeting Discussion and FDA Review

Proportion of Time FDA Followed Through on Matters Discussed/Directed



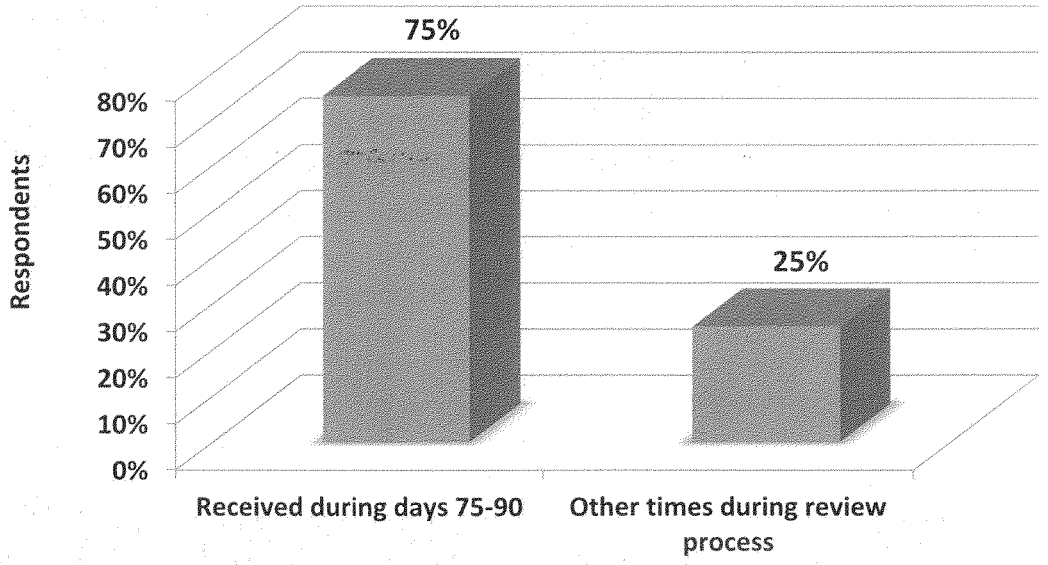
NORTHWESTERN UNIVERSITY

Interaction: Questions/Requests for Information



NORTHWESTERN UNIVERSITY

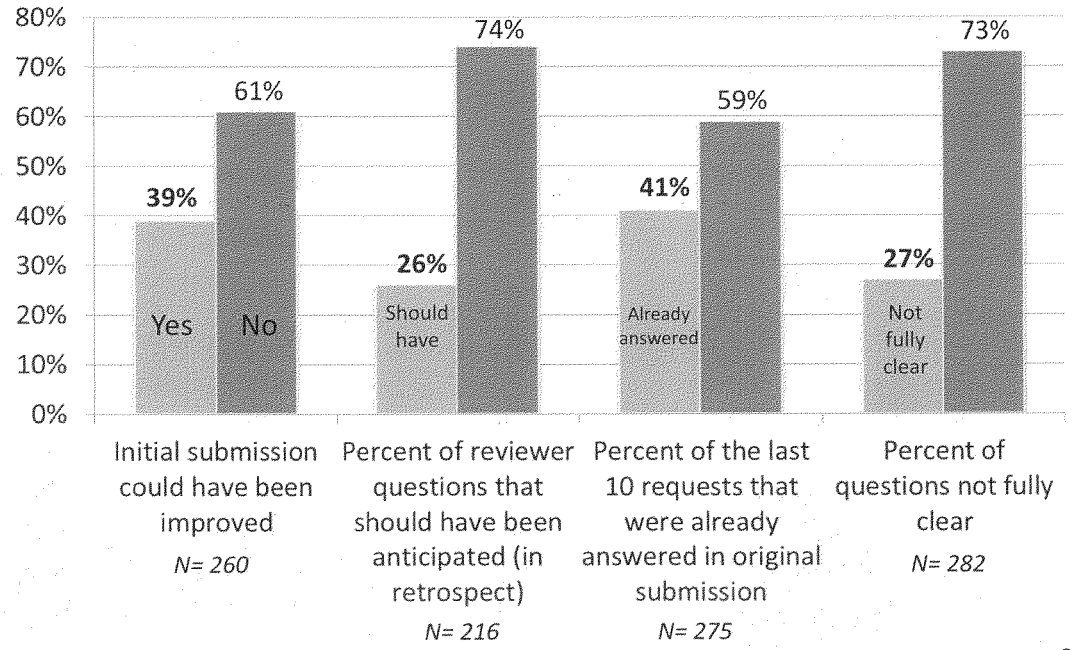
Percent of Requests for Information Obtained During Days 75-90 of FDA's 90-day Review Period



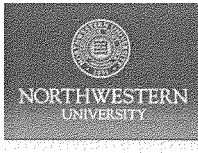
N= 293

NORTHWESTERN UNIVERSITY

Interaction: Respondent's Perspective



Key Findings
Different Impact on Large and Small Companies



Key Differences between Large and Small Companies

	Small Companies	Large Companies
New product (vs. line extension) [%]	**72%**	**35%**
SE Decision [%]	**61%**	**88%**
NSE Decision [%]	**13%**	**6%**
Interaction with FDA during development process	**earlier**	**later**
Pre-submission meeting with FDA sought	**39%**	**17%**
Duration of pre-IDE process [months]	**10.8**	**7.4**
Change in lead reviewer [%]	**19%**	**10%**
Total avg. review time [days]	**330**	**177**

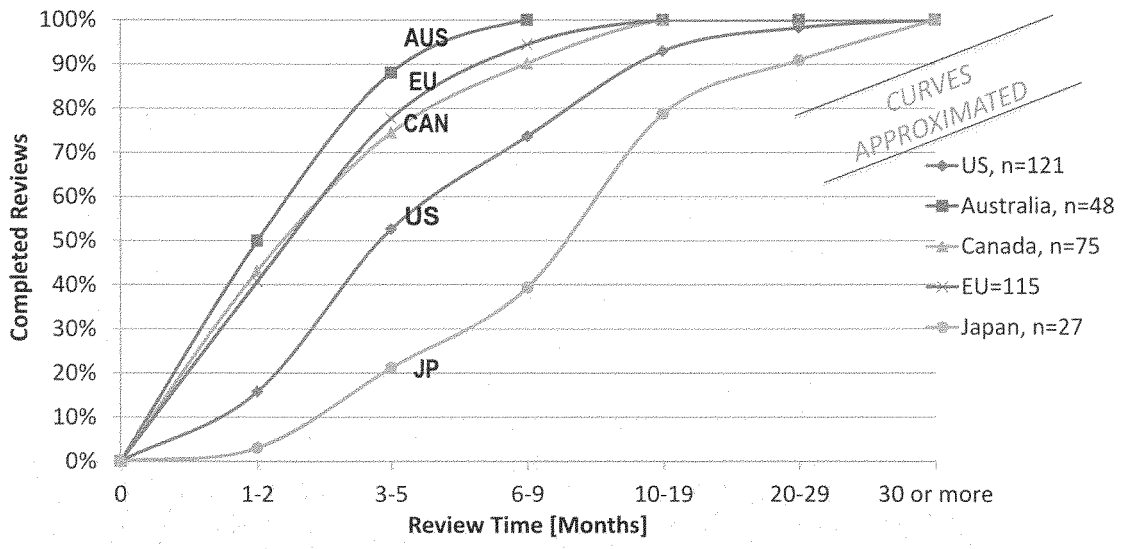
NORTHWESTERN UNIVERSITY

Key Differences between Large and Small companies

Respondents perceive:	Small Companies	Large Companies
Major difference with FDA's risk assessment [%]	**48%**	**23%**
% of FDA requests already answered in original submission	**53%**	**33%**
% of FDA requests "scientifically justified"	**30%**	**42%**
FDA requests having major effect on time [%]	**45%**	**36%**
FDA requests having major or medium effect on financial resources [%]	**76%**	**64%**

Key Findings
International Comparison

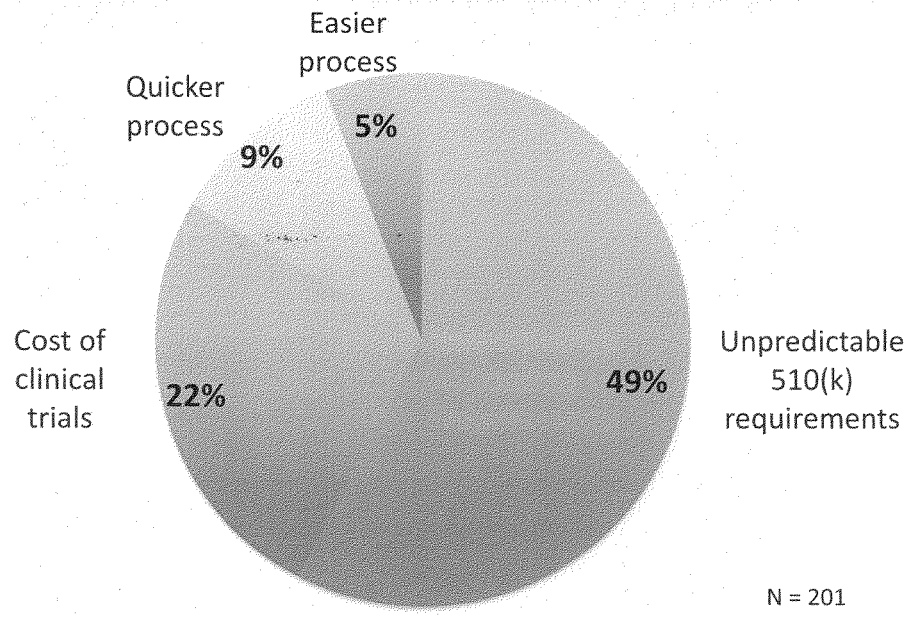
Comparison of International Review Time from Submission to Clearance/Registration



Length of review process in months (based on data points for "1-2", "3-5", "6-9", "10-19", "20-29", "30+ months" for the various regulatory systems. N per country: see above. Graph shows ultimately cleared/registered devices only.

NORTHWESTERN UNIVERSITY

Major Reason to Bring a Device OUS First



Within the last 3 years, if your company chose to first bring to market a specific device OUS, what was the major reason?

NORTHWESTERN UNIVERSITY

International Comparison between EU and US

	EU	US
Considered "most predictable regulatory system" [%]	**64%**	**8%**
First regulator/"body" approached to discuss and plan submission [%]	**80%**	**4%**
Review time (submission to decision) for products not requiring clinical data [months]	**2.7**	**5.9**
Review time (submission to decision) for products requiring clinical data [months]	**4.8**	**13.2**

Moving Forward to Foster Innovation and Timely Patient Access to Safe & Effective Technologies

NORTHWESTERN UNIVERSITY

Opportunities

Enhance predictability

- Increase number of guidance documents
- Timely update of guidance documents
- Clear and timely communication of *new* FDA expectations before publication in guidance

Increase process consistency

- Increase training (particularly implementation of current regulations)
- Reduce perceived differences in agency follow-through (by enhanced communication)
- Reduce reviewer turnover

NORTHWESTERN UNIVERSITY

Opportunities

Ensure efficient review process

- Preparation of clear and complete submissions
- Eliminate repeat requests of information already provided
- Timely access to meetings
- Increased use of interactive review concept

Close gap with international systems

- Continued harmonization efforts (GHTF)
- Sharing best practices (particularly on process side), while acknowledging differences in regulatory requirements

Opportunities

Increase attention to specific needs of small companies (while maintaining a level playing field)

- Improve opportunities for interaction
- Provide training support in areas where small companies tend to face particular challenges

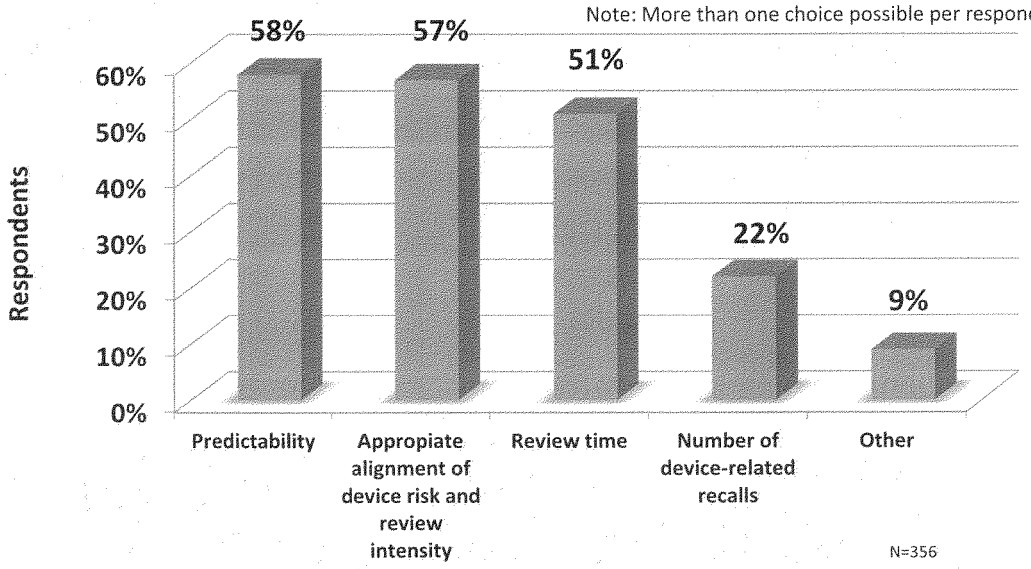
Monitor effect of process changes

- Evaluate impact of any process changes through appropriate performance metrics
- Work with industry to monitor process performance over time

NORTHWESTERN UNIVERSITY

Respondent-Suggested Metrics to Evaluate Future Changes in the 510(k) Process

Note: More than one choice possible per respondent.



Assuming that the FDA will make changes to the 510(k) clearance process, what primary metrics should be used to evaluate the overall performance of the revised 510(k) process?

Concluding Remarks

NORTHWESTERN UNIVERSITY

Funding Source

NORTHWESTERN UNIVERSITY

Outreach Partners

RAPS REGULATORY AFFAIRS PROFESSIONALS SOCIETY

Making better healthcare products possible℠

AdvaMed

DeviceAlliance

MassMEDIC

MDMA

Medical Device Summit

MICHBIO

MPO

Medical Design.com

ODT

onemedplace

STANFORD biodesign

eZASSI

Survey partner: ReadexResearch

Experienced. Trusted. Insightful.

Research Team

Investigators:

John H. Linehan, Ph.D.

Jan B. Pietzsch, Ph.D.

Research Team:

Marta G. Zanchi, Ph.D.

Abigail Garner, M.S.

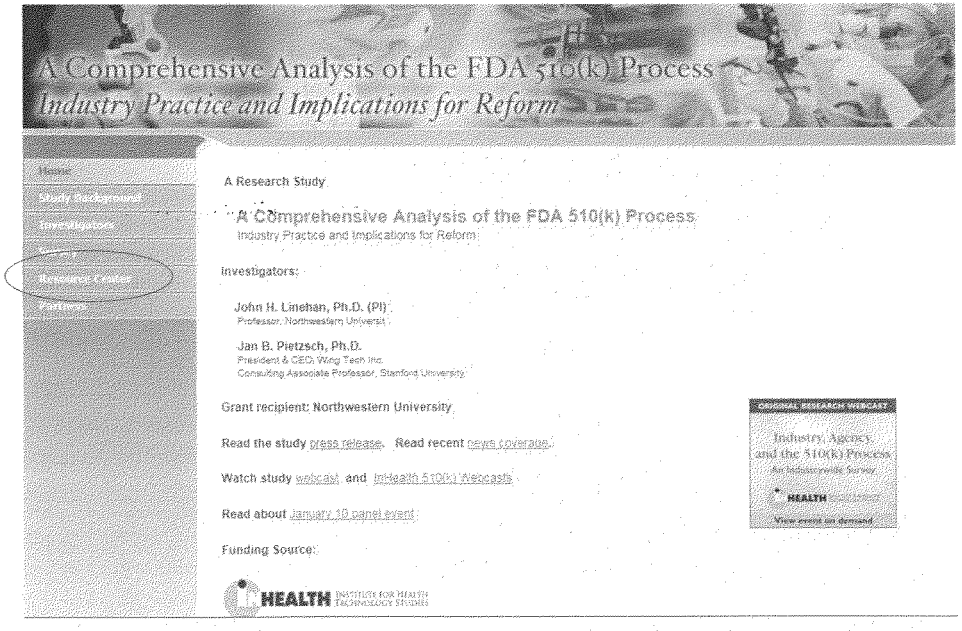
Remy Durand, M.S.

Brett Kuekan, M.S.

Sarah Kurihara

NORTHWESTERN UNIVERSITY

Study website @ www.510k.net



NORTHWESTERN UNIVERSITY

Resource Center @ www.510k.net

- 510(k) Basics
- FDA, Government and Medical Devices
  CDRH, ODE and OIVD documents, Medical Device User Fee and Modernization Act (MDUFMA) and US House of Representatives: Committee on Energy and Commerce
- FDA Guidance Documents relating to 510(k) regulatory process
- Workshops & Conferences - Webinars, TownHall and Public mtgs
- Literature - published articles pertaining to 510(k) process
- FDA Training and Continuing Education Courses
- Institute of Medicine of the National Academies (IOM)
  Links to agendas, webcast, presentations and reports from Meetings 1, 2 and 3 relating to 510(k)
- International Regulations

Respondents' Panel

Susan Alpert, MD, PhD
Former Senior Vice President and Chief Regulatory Officer
Medtronic Inc.

Peter Barton Hutt
Senior Counsel
Covington & Burling LLP

Philip J. Phillips
President
Phillips Consulting Group LLC

Jeffrey E. Shuren, MD, JD
Director
FDA Center for Devices and Radiological Health

HEALTH INSTITUTE FOR HEALTH TECHNOLOGY STUDIES

Thanks for Attending

Review the archived version of this webcast by visiting

www.inhealth.org/510ksurvey

To learn more about InHealth-sponsored research, visit the InHealth Web site at www.inhealth.org.

INHEALTH INSTITUTE FOR HEALTH TECHNOLOGY STUDIES

Ms. DEGETTE. Mr. Chairman.

Mr. STEARNS. Yes?

Ms. DEGETTE. Also, just to clarify, attached to our memo are two letters, one from the—five, sorry—four—some number—five letters supplementing that.

Mr. STEARNS. All right. By unanimous consent, that is so ordered.

And now we will go to the gentlelady, Sue Myrick is recognized for 5 minutes.

Mrs. MYRICK. Thank you, Mr. Chairman.

Dr. Fischell, I would like to just cover a couple things with you. Thank you, all of you for being here today and your testimony, by the way. You have been doing this for a long time, not just innovating but helping patients, et cetera, and a comment was made a little while ago about European inconsistencies and standards, I believe by Dr. Curfman. You have been talking, all of you, kind of about the fact that, you know, the Europeans are doing things quicker and we are taking a lot longer. Do you feel from what you have had experience with over the years and looking at the European standards that there is a lot of inconsistencies and that they are not doing a good job?

Mr. FISCHELL. No, I don't think that is the case, and I would like to once give the example of the migraine device. When we showed to the European notified body that we had done a clinical trial that proved it was safe and effective in the treatment of migraine, when we showed that there was already an FDA-approve device used for many years that had 20 percent stronger pulses and 30,000 times more and that was approved, it seems to me that the Europeans were logical in saying it is now approved for use in Europe. That seems logical to me.

Mrs. MYRICK. Well, and the other thing was, and Dr. Curfman, you said sometimes they are just a few months to a year behind. They have been waiting since 2006 for approval of that particular machine, which is a little longer than a few months to a year. But anyway, I wanted to ask you another question because you mentioned when you talked about the innovation and people going overseas and whatnot, if you were starting out today, would you still be able to find the same availability of funding for what you are doing? Because you mentioned something about funding in your remarks.

Mr. FISCHELL. We have—a month ago a venture capitalist said they would not give us the last money we need to get this product approved, the migraine product in the United States, because the FDA approval process is so risky that they would not risk the capital. We have worked with VCs over many years and we were well funded to do our stents, to do our defibrillator and pacer. They are no longer funding us. It is a real struggle now to get the funds to do the innovation, to make the jobs in America because the FDA has scared the venture capitalists.

Mrs. MYRICK. Well, and that brings me to another point. We have got over 40 device manufacturers in Charlotte alone, where I am from. North Carolina has a tremendous number because of all the medical there, you know, device manufacturers which is creating jobs. They pay well and, you know, the delays in approval are

keeping these jobs from being created here in America and so, you know, to me, this has a tremendous impact on what is happening here, what the FDA does relative to us being able to create those jobs that are obviously being created in other countries instead of here.

Mr. FISCHELL. You know, a migraine company only has 12 people employed and yet we are now hiring people in Europe to get it out into the population there. That doesn't make an American happy.

Mrs. MYRICK. No, it doesn't make any of us, very frankly.

Ms. Conger, I would like to ask you because of, you know, we know that the job of FDA is to make things safe. None of us are trying to say you shouldn't have safe devices and they should be effective, but they are supposed to also foster innovation, and just from our perspective, what do you think the balance should be between those two in how the FDA is running.

Ms. CONGER. Based on my research about other approval methods and their successes and failures, and I compare it to our current overly bureaucratic, overly politically worried system. We can have all three. We can have safety, reasonable safety, efficacy and innovation if we were using parts of models of other countries that are doing it so well. We have the opportunity to take the learnings of others, add it to the gems we know we do well, and come out with a better system. As it is set up now, it is not going to work.

Mrs. MYRICK. Can I quickly ask, Dr. Ianchulev, you worked in both systems relative to the European standards. I would just like your comment.

Mr. IANCHULEV. Yes. Actually, I am licensed in Europe as well as a physician and to me that has been—when I came to this country almost 20 years ago, I came here to innovate and practice cutting-edge medicine, and I have seen to my surprise that a lot of my European colleagues now have more advanced experience than what I can get here and deliver to my patients. And I have experienced the review process on the regulatory side in Europe and I would say that I haven't noticed it to be irrational nor have I heard from my colleagues or patients in Europe to feel that the environment is unsafe. At the same time, I should say that we don't have to rubber stamp something. It is a matter of looking at this is not a bearing point and another way to benchmark ourselves to find something that works for us and for our patients.

Mrs. MYRICK. I appreciate it. Thank you, Mr. Chairman.

Mr. STEARNS. I think just to confirm what you indicated to the gentlelady, over in Europe they have more advanced experience, you said?

Mr. IANCHULEV. In my field, for example, we have a lot of medical devices that we use, mainly new types of intraocular lenses, and to be more specific, there are other ones right now, new minimally invasive treatments for eye diseases such as glaucoma, and it is interesting that on the device side on the European side, you can see access to those technologies and experience in the hands of physicians, which is probably the only true way to appreciate not just read an article in a journal but really to have experience with the device. That is what physicians need to understand it.

I think on the drug side, it is opposite. I have noticed a lot more experience happens first here and then travels to Europe, and that

was my experience with Lucentis why we got it approved here and followed one year later there. It is just my personal experience is——

Mr. STEARNS. OK. Thank you.

The gentleman from Texas is recognized for 5 minutes, Mr. Green.

Mr. GREEN. Thank you, Mr. Chairman, and I would like unanimous consent to have a statement placed into the record, and I do have concerns because I know medical device companies who produce in our countries but there are rules particularly in Europe that they can't market a device there that is not admitted into the home country so they end up having to move their production facilities to another country. We may not want to lower our standards to the European standards, because I am going to ask Dr. Curfman some questions about that, but Dr. Curfman, I understand actually in some cases FDA is much quicker than in Europe on the reviews. Can you outline some of the concerns with the medical device approval system in the European Union?

Mr. CURFMAN. Well, I think again the most important thing in a review process is to ensure that a new device or a new drug is actually going to result in a better health outcome for the patient.

Mr. GREEN. And Europe doesn't require that?

Mr. CURFMAN. Europe doesn't require that. We do. And I think that that is really a fundamental difference in the two processes.

Mr. GREEN. And the structural way that the FDA does our approval but in Europe from what I understand, there are 74 for-prof-it entities that actually can be—you can almost cherry pick who you want to take your device to. Is that correct?

Mr. CURFMAN. That is correct.

Mr. GREEN. And the European Union allows any of those 74 to make that determination that the FDA does in our country?

Mr. CURFMAN. That is correct.

Mr. DINGELL. If the gentleman would yield, those things are called forum shopping over here.

Mr. GREEN. Oh, I understand. But that gives the companies—and I am amazed that Europe doesn't have some more quality control on what they do, but that is beside the point. Can you continue about the difference between us, the United States requirements under FDA and in Europe?

Mr. CURFMAN. Well, I think another point that we touched upon briefly is the issue of transparency, and that is putting information out to the public, getting it up on a Web site. The FDA does a beautiful job of that. The FDA's Web site is highly sophisticated, very deep in information. That doesn't exist in Europe.

Mr. GREEN. In our country, if someone is wanting to use a device, it is available, the information from the FDA because it is public record.

Mr. CURFMAN. That is correct.

Mr. GREEN. But those 74 entities, I understood from earlier testimony that that is proprietary information.

Mr. CURFMAN. That is proprietary information, and there is no information about who the decisions are being made, what the process was, who the people were who were involved in making

those regulatory decisions. In the FDA, that is all very transparent. You know exactly who did what.

Mr. GREEN. Well, I understood a statement earlier, and you wouldn't believe it from our panel today that the FDA is actually faster then the European Union on devices. Do we have a percentage or has anyone looked at that? And if somebody has some other—I want to hear Dr. Curfman first because he is in the business right now. Is that information that is readily available?

Mr. CURFMAN. I would imagine that Dr. Shuren would have that information probably more than I would.

Mr. GREEN. Well, Mr. Chairman, hopefully we can get that. Again, it sounds like we are comparing apples and oranges with results.

What are the problems with abandoning the effectiveness criteria for medical device approval in moving to the European standard?

Mr. CURFMAN. Well, you know, in medicine and health care today in the United States, we talk about evidence-based medicine. This is the core of our process in finding new therapies. New therapies need to be supported by real evidence, by clinical trials, by scientific data, not just casual impressions that they work in that patient so they will work in every patient but real solid clinical trials, and doing clinical trial is very difficult but we have gotten in the United States very good at it. It has become a very refined science so that we can get very good and precise answers to these questions about whether new drugs and devices really work by helping people's health. We can do that today.

Mr. GREEN. I only have about 26 seconds. In Europe, if I was a medical device company and hired one of those entities, those for-profit entities to do it, that patient wouldn't be able to know anything about how the clinical went. Is that proprietary information in Europe?

Mr. CURFMAN. Yes, not only the patient but physicians. Nobody would really know that. There is no way to get it. And if you try to get it, they simply say it is proprietary information, we won't release it. It is astonishing that that would be allowed to happen because it is so strikingly different here.

Mr. GREEN. Thank you, Mr. Chairman.

Ms. SAGAN. Mr. Chairman, I feel compelled to ask to be able to make a statement. I am sorry. In terms of the low-glucose suspend insulin pump, there is no safety issue. It is not safe to not allow the low-glucose suspend system to come into being, into practice in the United States. If you understand type 1 diabetes, it is too dangerous to allow insulin to be pumped into a body that is experiencing low blood glucose, more dangerous than running a 90-minute period of running high glucoses. My daughter's glucose level has been at 500 many, many, many times, and the long-term complications of high sugars are far diminished by the short-term complications.

Mr. GREEN. I thank the gentlelady.

We have a request that we recess our committee. We are doing some votes in another subcommittee, and the chairman has asked that I recess the committee temporarily so that all members could go to this other committee, so with your indulgence and forbearance, I would appreciate your waiting, and I tell all members that

we are going to recess the committee and we will try to get back shortly.

[Recess.]

Mr. STEARNS. The subcommittee will reconvene, and I thank all of you. If the witnesses would please come to the table again, we will start the questions here, and we were able to receive a unanimous consent agreement that the votes at this other committee will be rolled until after our votes in the House, which will probably occur between 1:15 and 1:30. So I don't want to hold up the witnesses here anymore.

Are Mr. Mandel and Dr. Ianchulev close by? I just want to make sure—they can't be far. I think under the time constraints we have, I think we will start with the gentleman from Georgia, Mr. Gingrey, for questions and we will just keep moving forward here. So the gentleman is recognized for 5 minutes.

Mr. GINGREY. Mr. Chairman, thank you. Thank you very much. I am going to confine my questions and remarks to Dr. Curfman. Dr. Curfman, of course, as executive director of the New England Journal of Medicine and a cardiologist, I too am an M.D., as you know, and certainly it is an honor have you come before the committee to testify, and we thank you for being here today, as we do the other witnesses. I think you have been very patient and you have been very good with us.

Dr. Curfman, in your testimony, you state your support for, and I quote "high-priority innovation in medical devices" but conclude that the glamour of innovation does not always work for patients if we cut corners in quality control. Is that a fair assessment?

Mr. CURFMAN. Yes, that is exactly right.

Mr. GINGREY. As examples of cutting corners in quality control, your testimony focuses on two products that you say ran through the 510(k) fast-track process versus the more rigorous premarket approval process. Had the Sprint Fidelis defibrillator gone through the more rigorous PMA, that premarket approval, versus the 510(k), do you believe that some patient injuries might have been avoided?

Mr. CURFMAN. I think that probably the way to have done that would be to phase it in rather than doing a clinical trial, that instead of launching this into many thousands of patients in a short period of time, to set some benchmarks for the lead in a limited number of patients and try to see if any problems were emerging there. The problem with this lead was that it was made quite a bit thinner than previous leads, and it was——

Mr. GINGREY. And in your testimony, you said that that approval process of Medtronic's Sprint Fidelis lead was fast-tracked, it was through that 510(k) process.

Mr. CURFMAN. Yes. There was no clinical testing. So what I would propose is that there be some clinical testing——

Mr. GINGREY. Right. Well, I understand that.

Mr. CURFMAN [continuing]. In a limited number of patients.

Mr. GINGREY. I want to ask you this, because I am holding in my hand a PMA record, premarket approval record, number P920015 for the Medtronic's Sprint Fidelis lead dated 2007, which in fact means that the Sprint Fidelis product did go through the more rigorous PMA supplement process and not the 510(k) as your testi-

mony suggests. Are you aware that your testimony on this is factually wrong?

Mr. CURFMAN. I don't think it is wrong.

Mr. GINGREY. Well, here it is.

Mr. CURFMAN. Well, I would have to——

Mr. GINGREY. Let me just follow up on that, and maybe you can check your notes or maybe talk with your secretary or whomever gave you this information. Your testimony also cites the federal preemption for medical devices that prevented U.S. patients from suing Medtronic. Doctor, the federal preemption for medical devices only applies to class III products that go through the PMA process, not those that go through 510(k). The fact that this reality did not raise a red flag for you when drafting and reviewing your testimony here today is troubling, to say the least.

The second example you cite in your testimony as proof of 510(k) failure is this metal-on-metal hip. Dr. Curfman, the Safe Medical Devices Act of 1990 directed the FDA, and I will say that again, this act directed the FDA to review certain class III devices and to ascertain whether they should be reclassified and go through this premarket approval process, so-called PMA, as I held up on the other one with Medtronic. One of these devices is the metal-on-metal hip yet 20 years later the FDA has yet to conduct a review. So it appears that the failure of this product is not due to 510(k) process but to regulatory inaction by our own FDA. So Dr. Curfman, do you believe that the FDA should follow the direction of Congress and implement the Safe Medical Devices Act of 1990 in order to better protect patient safety?

Mr. CURFMAN. Well, I think that it is important for some of these previously approved devices to be looked at again, and——

Mr. GINGREY. Indeed, that is what the 1990——

Mr. CURFMAN [continuing]. I would support that.

Mr. GINGREY [continuing]. Act called for.

Mr. CURFMAN. That is correct. Yes, exactly. So I think that it should be done selectively but I think that some of these previously approved devices do need to have another look.

Mr. GINGREY. Well, absolutely, and I agree with you completely, Dr. Curfman, and I think we could have avoided some huge problems if that had been done. Both instances you cite to support the failure of this 510(k), the fast-track process, appear to be either inaccurate or factually incorrect, and with all due respect, these inaccuracies call into question, I hate to say it, but, you know, as a distinguished doctor and executive editor of one of our most distinguished medical journals, the New England Journal of Medicine, these little simple inaccuracies call into question what you describe as your careful analysis of these two studies you reference in your testimony.

Mr. CURFMAN. No, I disagree, Dr. Gingrey. I think that everything that I have said is accurate. I point out to you that the Sprint Fidelis lead was removed from the market in 2007. This document that you have given me is dated 2007. So something doesn't quite add up here. It was pulled from the market in 2007 by Medtronic. So I am not sure what this document——

Mr. GINGREY. Well, I would be happy—I think my time is expired.

Mr. STEARNS. The time has expired.

Mr. GINGREY. Doctor, I would be happy to have you follow up with written testimony to the committee.

Mr. CURFMAN. I would be happy to do that.

Mr. STEARNS. I think the gentleman from Georgia——

Mr. GINGREY. If there are some corrections that you would like to put into the record, we would be glad to put that into the record.

Mr. CURFMAN. I would be happy to do that.

Mr. STEARNS. Dr. Gingrey, if you feel comfortable, you could also ask him questions and we can ask him to reply for our record too.

With that, I recognize Ms. Christensen——

Mr. GINGREY. Thank you, Mr. Chairman. I yield back.

Mr. STEARNS [continuing]. For 5 minutes.

Mr. CHRISTENSEN. Thank you, Mr. Chairman, and I want to thank the panelists, especially those who are patients or representing patients. I think everyone up here felt your pain. And just before I ask my question, I just wanted to say that I understand that despite all of the comparisons between Europe and the United States, I still understand that the U.S.-based companies dominate the industry globally, medical device industry, and it is also interesting to note that the medical device industry is one of the few sectors with a positive trade balance today in our struggling economy.

Dr. Curfman, it seems like you are getting all of the questions today. I would like to ask you about the effect of regulation on innovation within the medical device technology field. In your written testimony, you stated that innovation is essential—I am quoting you here—"innovation is essential to the future or our Nation's health but innovative medical products cannot succeed unless they are both effective and safe." Can you explain how innovation in the medical field is fostered by sensible quality safeguards?

Mr. CURFMAN. Yes. Thank you, Dr. Christensen. I think that real innovation, real innovation needs to involve products in which the efficacy has been clearly demonstrated and the safety has been clearly demonstrated. Otherwise it is not real innovation. We have talked about creating jobs in the medical device industry, and I think we all feel that that is a very important goal, but we don't want jobs to be created to create defective medical devices that don't work, that cost a lot of money, that pull money out of our health care system that could be better used in other ways on things that do work or on devices that are not safe. So this is why I have tried to make a case that an important part of innovation is to really establish that the product works and that it is safe and that if you don't do that, it is not real innovation.

Mr. CHRISTENSEN. FDA must—and we have to support them in protecting the health and safety of millions of patients in our country, and the agency can only accomplish this when novel drugs and new devices are rigorously evaluated for safety and efficacy. In your opinion, do manufacturers always take appropriate premarket steps necessary to protect patient safety?

Mr. CURFMAN. In my experience, they do not always do that, and that is why oversight is necessary. That is why regulation is necessary. That is why it is important for third parties to be taking

a look at these products and doing some oversight and ensuring that efficacy and safety are really established.

Mr. CHRISTENSEN. So that must contribute to some of the delays as well?

Mr. CURFMAN. It does. There is a process involved. It does take time. I am sure that these delays can be reduced. I think that that should be a goal of the FDA. But that doesn't mean that the process should be eliminated.

Mr. CHRISTENSEN. Well, many have criticized, and we have heard it today, FDA for stifling innovation with their rules and regulations concerning medical devices. In your opinion, has FDA made the approval process for medical devices too onerous for medical device manufacturers?

Mr. CURFMAN. My experience with the FDA is that they are keenly interested in innovation. They are keenly interested in improving the lives of patients. They want to get products to market. That is my sense. At the same time, they know that a process establishing efficacy and safety is a critical part of that process.

Mr. CHRISTENSEN. Well, are there ways that the FDA could strengthen some of the aspects of their approval process?

Mr. CURFMAN. Well, as Congressman Waxman said, in order to do that, they need resources. So I think that the first thing is that we can't cut their budget and expect them to improve their processes. There is just a disconnect there. So I think we need to look at the budgeting process and be sure that they have the resources that they need to do the job.

Mr. CHRISTENSEN. Thank you. And I think more than ever now, we need to make sure we are making smart choices on the budget and cuts to FDA as we have done already make no sense. They really hurt patients. They hurt companies that want to bring innovative drugs and medical devices to the market. Thank you. I am out of time.

Mr. STEARNS. I thank the gentlelady.

I think by mutual agreement, we are going to the gentleman from California, Mr. Bilbray. You are recognized for 5 minutes.

Mr. BILBRAY. Thank you, and I appreciate the doctor's questions. I think the delegate from the Virgin Islands has a background here. You know, we have got some indicator species here as we say in the environmental community that are not being observed, and that is, the venture capital that goes into this innovative technology. It is not—you know, by the time it gets to the FDA, it is at the end of the line, and I just want to say right now, July 11, everybody is put on notice, 50 percent of the venture capital investment in medical devices and research has dropped off in my region. Now, that is the krill of medical breakthroughs, and, you know, when the krill dies, in a few years you are going to say well, what happened, why isn't there any new information. Because the big guys use that krill to feed on. So there is a concern here that we may be contributing to the extinction of a species that we take for granted but it essential in the food chain of medical breakthroughs.

Dr. Curfman, I have got a question for you. Do you believe the defibrillators that we have got out in the public are as effective in the hands of a layman as they would be in a trained physician?

Mr. CURFMAN. You are talking now about defibrillators——

Mr. BILBRAY. The defibrillators——

Mr. CURFMAN. The manual defibrillators?

Mr. BILBRAY. The manual defibrillators.

Mr. CURFMAN. Well, the automatic external defibrillators can be operated by a layperson with only a small amount of training, and they are designed to do that and they can certainly be lifesaving.

Mr. BILBRAY. But they can be lifesaving. We agree with that.

Mr. CURFMAN. Yes.

Mr. BILBRAY. But do you think that they are just as effective in a layman's hands as it would be in a trained cardiologist's hands?

Mr. CURFMAN. Well, you need some training to use these. They are not totally intuitive. If you have never, never used one, you are going to have to figure it out. They are certainly a lot easier than older ones.

Mr. BILBRAY. Do you have any idea how long it took us to finally approve this and get it out in the field?

Mr. CURFMAN. Well, it took some years, yes.

Mr. BILBRAY. OK. Do we have any idea of how many people died of cardiac arrest in public during that period? We don't have any idea at all. But we can only imagine.

You know, I have just got to say, we talk about the morning sickness medicine of the 1950s that caused birth defects, and that is what you remember as the chairman emeritus said. They don't think about Benedictine in the 1980s that was perfectly safe but driven off the market, and a lot of it was because you remember the stuff when it goes bad but you don't think about all the savings, and I think we all agree. Aspirin, classic example, hundreds of people die every year, and it has probably done more to help with health of probably any device

My question is this. When we talk about the device that Mr. Mandel talked about and with 3 percent increase annually in child melanoma annually since the 1970s, we have got a device that physicians could use that may help in that application but because it cannot be proven to as effective as a dermatologist, don't you think we have got to start talking about reality, that early detection is the most essential part of surviving melanoma. Wouldn't you agree?

Mr. CURFMAN. Absolutely.

Mr. BILBRAY. And why would we say that we do not want to give a device to general practitioners that see the overwhelming majority of children—why would we as an agency say this should only be used at the back end of the process, dermatologist, after the general practitioner has sent them over?

Mr. CURFMAN. Like any device, the efficacy needs to be established. This is a device where there are probably not going to be any safety issues but there are efficacy issues. It is a device that costs money. It has to be shown to be accurate.

Mr. BILBRAY. Costs money.

Mr. CURFMAN. It has to be accurate. It has to work and it has to be shown to work.

Mr. BILBRAY. But——

Mr. CURFMAN. And the evidence has to be there, and if you don't have the evidence, you can't just approve the device.

Mr. BILBRAY. But if you have the evidence to apply——

Mr. CURFMAN. You need the evidence. You need the evidence in a real clinical study.

Mr. BILBRAY. Excuse me. But if the technology works for a dermatologist, OK——

Mr. CURFMAN. Who says? That is the point of doing clinical studies, to get the evidence.

Mr. BILBRAY. OK. Let us back up then. The same clinical trials that say you apply, why would you shift it? If it works good for a dermatologist and it works, why would a bureaucracy, why would a government agency say we don't want this to be applied at the general practitioners, we are going to make a judgment call that we want it to be applied for dermatologists. Now, don't you agree as the manual defibrillators but especially with melanoma, that early detection, if there is an opportunity, early detection with general practitioners, that is an essential part of treating that disease and addressing that disease and that is prevention. The earlier the better, right?

Mr. CURFMAN. Absolutely.

Mr. BILBRAY. OK.

Mr. CURFMAN. So what you need to do is show that the device detects it earlier and improves patient outcomes.

Mr. BILBRAY. OK. If you wanted to prove that, then why would you not allow a review board to look at this and review it? Why would you say we are not going to allow a review board to take a look at this and review it?

Mr. CURFMAN. I think that you have to have the proper data in hand for the review board to look at, and I am not completely familiar with this device so I can't really say how much data they had, but I am assuming that they don't have enough data for the review board to review it.

Mr. BILBRAY. And let me just mention, Mr. Chairman, I think the one we asked about that has been brought up here, do you agree that we had a great success in the 1990s with AIDS by allowing patients to sit on the review boards? Do you think that diabetics and cancer patients should have the same opportunity in this century as we gave in the last century to AIDS patients?

Mr. CURFMAN. Yes.

Mr. BILBRAY. Thank you, Mr. Chairman.

Mr. STEARNS. I thank the gentleman. His time is expired.

Panel, we are going to ask one more 5 minutes and then you will be excused, so we will finish.

Mr. Griffith is recognized for 5 minutes.

Mr. GRIFFITH. Thank you, Mr. Chairman. I would like to yield 3 minutes of my 5 minutes to Mr. Gingrey and then 2 minutes to Mr. Lance.

Mr. STEARNS. So ordered.

Mr. GINGREY. Well, I thank the gentleman for yielding time to me. I wanted to, during the last discussion when my 5 minutes expired and I was talking with Dr. Curfman, I had a question for Mr. Fischell. On that note, I want to return to you fairly quickly. Given my concerns, Mr. Fischell, with the testimony of Dr. Curfman, I was wondering if you could share your thoughts on the veracity of those two studies that were outlined in Dr. Curfman's testimony.

He didn't think too highly of them. Could you give us your opinion on those studies?

Mr. FISCHELL. I am not an expert on that, and I think that they were PMA supplements, which are treated differently from PMAs, and I think that may account for some of the difference here. But I am by no means an expert on that subject.

Mr. GINGREY. Well, I appreciate your honesty on that. The PMA supplement is reviewed in those articles using the same standard as the original postmarket analysis, PMA. So I want that to be in the record and I want that statement to be in the record.

In the last minute or so that I have before I think my friend wants to yield to another colleague on this side of the aisle, look, I think we are all here for the right reasons. There is certainly a difference of opinion on one end of the table from most of the other witnesses in regard to the FDA and are they doing their job in a most efficient, timely manner that is safe for patients. Obviously, as Dr. Curfman pointed out, safety is hugely important, but to make it so difficult losing venture capitalists, we are losing research and development, we are losing new products to the European Union, and then they come back over here and finally get to our market but all the jobs——

Mr. STEARNS. The gentleman's time has expired.

Mr. GINGREY [continuing]. Are gone. That is what this is all about, and I thank the gentleman for yielding to me and I yield back.

Mr. STEARNS. The gentleman, Mr. Lance, is recognized for 2 minutes.

Mr. LANCE. Thank you very much. I will take 1 minute, and I appreciate the courtesies of my colleague, Mr. Griffith.

Dr. Fischell, I represent a district that is really the medicine chest of the country in north central New Jersey, more pharmaceutical and medical device employees than any other district in the United States. In your testimony, you state that beyond the adverse impact FDA is having on patient care, it is weakening the U.S. leadership position in medical technology innovation and as a result our economy. Would you comment briefly on that statement with which I agree and is so terribly important to the district I serve?

Mr. FISCHELL. Well, it has been very clear to me personally by the fact that from 20 to about 5 years ago, venture capitalists would come to me and say Dr. Fischell, I would like to support your latest innovation, tell me what it is. Now I have recently gone to venture capitalists and said we have this great new cure for migraine and I need another $2 million to finish it. They said because of the FDA, we can't give it to you, it is too risky. That is the difference.

Mr. LANCE. Well, thank you very much, and I appreciate having the opportunity to speak with you on that, and I yield back the balance of my time.

Ms. DEGETTE. I am wondering if Mr. Griffith would just yield to me for one brief moment?

Mr. GRIFFITH. One brief moment, I yield to the gentlelady.

Ms. DEGETTE. Thank you very much.

I just want to point out, there was a Bloomberg News article today that said venture capital funding for medical device and equipment makers gained 20 percent to $840 million in 90 deals over the last 3 months, so I think the record needs to reflect that there is still ample venture capital for medical devices as well as for all of biotechnology, and anything this committee can do to encourage that——

Mr. GINGREY. Mr. Griffith, would you yield to me for unanimous consent?

Mr. STEARNS. No, I think we are just going to wrap up here.

Mr. GINGREY. Mr. Chairman, I do have a UC request.

Mr. STEARNS. OK. Go ahead.

Mr. GINGREY. I would like to for unanimous consent request to submit for the record these materials that I am holding be inserted into the record, and it is important because these materials show that the Medtronic device that Dr. Curfman was talking about——

Mr. STEARNS. OK. I think what we will do is——

Mr. GINGREY [continuing]. Was approved through PMA and not the 510(k) process. That is all this does.

Mr. STEARNS. The minority needs to see it, and we also have here a quote from the New York Times——

Ms. DEGETTE. Reserve the right to object.

Mr. STEARNS [continuing]. And the LexisNexis also, so we have three items.

Let me close, and we are going to recess the committee and thank the panel for their very compelling testimony and we appreciate your forbearance, and so we will take up the second panel after the set of votes, and so the subcommittee is temporarily in recess.

[Recess.]

Mr. STEARNS. The subcommittee will come to order, and now we will proceed to our second panel, and Dr. Shuren, you have been very patient with us and we appreciate that, and we are glad to have Mr. Waxman with us as we proceed to the second panel.

With that, I will swear you in. Let me start by saying you are aware that the committee is holding an investigative hearing, and when doing so has had the practice of taking testimony under oath. Do you have any objection to testifying under oath?

Mr. SHUREN. I do not.

Mr. STEARNS. The chair then advises you that under the rules of the House and the rules of the committee, you are entitled to be advised by counsel. Do you desire to be advised by counsel during your testimony today?

Mr. SHUREN. I do not.

Mr. STEARNS. In that case, if you would please rise and raise your right hand?

[Witness sworn.]

Mr. STEARNS. You are now under oath and subject to the penalties set forth in Title XVIII, section 1001 of the United States Code. You may now give a 5-minute summary. Your written testimony will be part of the record. Proceed. Thank you.

TESTIMONY OF JEFFREY E. SHUREN, DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION

Mr. SHUREN. Mr. Chairman and members of the subcommittee, I am Dr. Jeff Shuren, Director, Center for Devices and Radiological Health, or CDRH, at the Food and Drug Administration. Thank you for the opportunity to testify today, and I would like to thank the participants on the first panel, who raised many important points that I agree with.

The mission of the FDA is to protect and promote the public health, to protect the public health by assuring that the devices that come on the market are safe and effective, and to promote the public health by facilitating innovation. Striking the right balance is challenging but also critical.

In September 2009, soon after I came to CDRH, we initiated a review of our medical device premarket review programs in response to concerns expressed by industry and others. We conducted and honest and frank self-assessment of these processes including the 510(k). In 2010, we released two reports which concluded that we had not done as good a job managing our review programs as we should, and proposed potential solutions for improvement. The number one problem we found was that there was insufficient predictability in our premarket review programs which contributes to inconsistent decisions and longer terms to market. We identified several root causes. They including changing, unnecessary, inappropriate and/or inconsistent data requirements imposed on device sponsors, insufficient guidance for industry, insufficient interactions between the agency and industry, very high reviewer and manager turnover at CDRH, turnover that is almost double that of FDA's drugs and biologic centers, insufficient training for reviewers, insufficient oversight by center managers, CDRH's rapidly growing workload due to the increasing scientific and technological complexity of the devices we reviewed and the number of submissions we received, and poor quality submissions by industry.

We solicited public comment on these reports from stakeholders and heard a wide range of perspectives. This past January, we announced 25 specific actions that CDRH will take in 2011 to improve the predictability, consistency and transparency of our premarket review programs, and have since announced additional actions. For example, we have made a commitment to develop a range of updated and new guidances to clarify CDRH requirements for timely and consistent product review including device-specific guidance in several areas such as mobile applications and artificial pancreas systems. We are also working to revamp the guidance development process to make it more efficient. We are enhancing the interactive review process and streamlining the review program for low- to moderate-risk novel devices called the de novo process. We are streamlining our clinical trial program to assure that clinical trials can start in a timely manner. We have already established a new center science council to help ensure consistency and predictability in our scientific decision-making, and we are creating a network of experts to help us resolve complex scientific issues and product assessment, which we hope will ultimately result in more timely reviews of device submissions. We are instituting a reviewer

certification program and a pilot experiential learning program to provide review staff, especially our newer review staff, with necessary training and real-world experiences.

These efforts signify our commitment to improving our premarket review programs to ensure that patients have timely access to safe and effective devices and the U.S. device industry remains strong and innovative.

Mr. Chairman, I commend the subcommittee's efforts and I am pleased to answer any questions the subcommittee may have.

[The prepared statement of Mr. Shuren follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

STATEMENT

OF

JEFFREY SHUREN, M.D., J.D.

DIRECTOR

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES

"REGULATORY REFORM SERIES #5 – FDA MEDICAL DEVICE REGULATION:
IMPACT ON AMERICAN PATIENTS, INNOVATION AND JOBS

JULY 20, 2011

Release Only Upon Delivery

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Dr. Jeffrey Shuren, Director, Center for Devices and Radiological Health (CDRH), at the Food and Drug Administration (FDA or the Agency). I am pleased to be here today to discuss CDRH's initiatives under President Obama's Executive Order 13563, Improving Regulation and Regulatory Review, and other activities we are undertaking to improve the predictability, consistency, and transparency of our regulatory processes.

The Impact of Regulation on Innovation

FDA is charged with a significant task: to protect and promote the health of the American public. To succeed in that mission, we must ensure the safety and effectiveness of the medical products that Americans rely on every day, and also facilitate the scientific innovations that make these products safer and more effective. These dual roles have a profound effect on the nation's economy. FDA's premarket review of medical devices gives manufacturers a worldwide base of consumer confidence. Our ability to work with innovators to translate discoveries into products that can be cleared or approved in a timely way is essential to the growth of the medical products industry and the jobs it creates. U.S.-based companies dominate the roughly $350 billion global medical device industry. The U.S. medical device industry is one of the few sectors, in these challenging economic times, with a positive trade balance.[1] In 2000, the U.S. medical device industry ranked 13th in venture capital investment—now, 10 years later,

[1] PwC (formerly PriceWaterhouseCoopers), "Medical Technology Innovation Scorecard" (January 2011) at page 8, available at *http://pwchealth.com/cgi-local/hregister.cgi?link=reg/innovation-scorecard.pdf*.

it's our country's fourth largest sector for venture capital investment.[2] And, the medical device industry has produced a net gain in jobs since 2005, even while overall manufacturing employment has suffered. According to a recent industry survey, "If you listen to what CEOs are saying, the industry should experience healthy growth in employee headcount in 2011" (Emergo Group, "Medical Device Industry Outlook" (December 2010), available at http://www.emergogroup.com/files/2011-medical-devices-industry-outlook-webinar-version.pdf).

As noted in a January 2011 report on medical technology innovation by PwC (formerly PriceWaterhouseCoopers), the U.S. regulatory system and U.S. regulatory standard have served American industry and patients well. As that report states, "U.S. success in medical technology during recent decades stems partially from global leadership of the U.S. Food and Drug Administration. FDA's standards and guidelines to ensure safety and efficacy have instilled confidence worldwide in the industry's products. Other countries' regulators often wait to see FDA's position before acting on medical technology applications, and often model their own regulatory approach on FDA's."

In terms of time to market, data show that the United States is performing as well or better than the European Union (EU). An industry-sponsored analysis[3] shows that low-risk 510(k) devices without clinical data (80 percent of all devices reviewed each year) came on the market first in the United States as often as or more often than in the EU. The EU typically approves higher-

[2] PriceWaterhouseCoopers/National Venture Capital Association, MoneyTree™ Report, Data: Thomson Reuters, Investments by Industry Q1 1995 – Q4 2010, available at *http://www.nvca.org*.
[3] California Healthcare Institute and The Boston Consulting Group, "Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry" (Feb. 2011), available at *http://www.bdg.com/documents/file72060.pdf*.

risk devices faster than the United States because, unlike in the United States, the EU does not require the manufacturer to demonstrate that the device actually benefits patients.

FDA also recognizes that, if the U.S. is to maintain its leadership role in this area, we must continue to streamline and modernize our processes and procedures to make device approval not just scientifically rigorous, but clear, consistent and predictable. I will discuss our efforts in that regard in more detail later in my testimony.

The President's Regulatory Reform Initiative

With Executive Order 13563, issued on January 18, 2011, President Obama laid the foundation for a regulatory system that is designed to protect public health and welfare, while also promoting economic growth, innovation, competitiveness, and job creation. An accompanying Wall Street Journal op-ed by the President highlighted FDA's medical device initiatives, described in greater detail later in this testimony, as an example of the kind of efforts he was talking about. Among other things, and to the extent permitted by law, the Executive Order:

- Requires agencies to consider costs and benefits of regulation to ensure that the benefits justify the costs and to select the least-burdensome alternatives;
- Requires increased public participation and an open exchange;
- Directs agencies to take steps to harmonize, simplify, and coordinate rules; and
- Directs agencies to consider flexible approaches that reduce burdens and maintain freedom of choice for the public.

The Executive Order also requires a government-wide "look back" at existing federal regulations to review significant rules and decide which should be streamlined, reduced, improved, or

eliminated. One of the goals of this approach is to eliminate unnecessary regulatory burdens and costs on individuals, businesses, and governments.

On May 18 of this year, the Department of Health and Human Services (HHS or the Department) released its Preliminary Plan. The Plan highlights regulations already being modified or streamlined and identifies additional candidates for further review.

In order to increase public participation in the retrospective review, HHS posted its Preliminary Plan for public comment at *http://www.hhs.gov/open/recordsandreports/execorders/13563/draft/index.html*. The comment period for HHS' Preliminary Plan closed on June 30, 2011. HHS will now proceed to finalize the Plan.

As a first step in the regulatory review, the Secretary asked each agency to do an inventory of its existing significant regulations to provide information that will assist the Department in constructing an ongoing retrospective review process. FDA sought comment on how the Agency could revise its existing review framework to meet the objectives of Executive Order 13563, regarding the development of a plan with a defined method and schedule for identifying certain significant rules that may be obsolete, unnecessary, unjustified, excessively burdensome, or counter-productive. FDA focuses its retrospective review efforts on regulations that have a significant public health impact and regulations that impose a significant burden on the Agency

and/or industry. FDA has under review, or has identified, over 40 rules as candidates for regulatory review.

On April 27, 2011, FDA published a notice in the *Federal Register*, requesting comment and supporting data on which, if any, of our existing rules are outmoded, ineffective, insufficient, or excessively burdensome and thus may be candidates for review. This docket closed on June 27. FDA is now reviewing the comments received and will be using the comments to inform its future regulatory review activities.

Detailed information about FDA's regulatory review activities can be found at

http://www.fda.gov/AboutFDA/Transparency/TransparencyInitiative/ucm251751.htm.

There you will also find some of the activities FDA is undertaking in support of Executive Order 13563. For example, in an effort to regulate based on risks and reduce regulatory burden, we are reviewing classifications of medical devices to determine if down-classification (i.e., moving a device to a classification with less stringent requirements) is appropriate. Two weeks ago, consistent with its commitment under the Medical Device User Fee Amendments of 2007, FDA issued draft guidance describing its intent to exercise enforcement discretion with respect to premarket notification requirements for 30 different *in vitro* diagnostic and radiology device types with well-established safety and effectiveness profiles. The devices include common urine and blood tests, alcohol breath tests, blood clotting protein tests, and radiology device accessories, such as film cassettes, film processors, and digitizers. We intend to exempt these

devices from premarket notification requirements through the appropriate regulatory processes. We will, of course, continue to enforce all other applicable requirements.

In addition, we are updating existing regulations, such as converting the device registration and listing process to a paperless system, allowing for the utilization of the latest technology in the collection of information, while maintaining an avenue for companies for which paper applications are more convenient.

We are instituting a paperless, electronic Medical Device Reporting system, which will speed reporting and analysis of adverse events and identification of emerging public health problems, as well as lower costs for manufacturers.

We are revising device premarket approval regulations (Special PMA Supplement Changes Being Effected) to remove duplicative requirements and to streamline and clarify regulatory requirements. And we will be proposing to allow the use of validated symbols in device labeling, without the need for accompanying English text, thereby reducing the burden of labeling requirements by permitting harmonization with labeling for international markets.

FDA's Medical Device Regulatory Reform Initiatives

Federal agencies have long had to consider the various impacts of regulations on industry and the public. The laws and guidance documents that FDA follows require it to measure the effect of

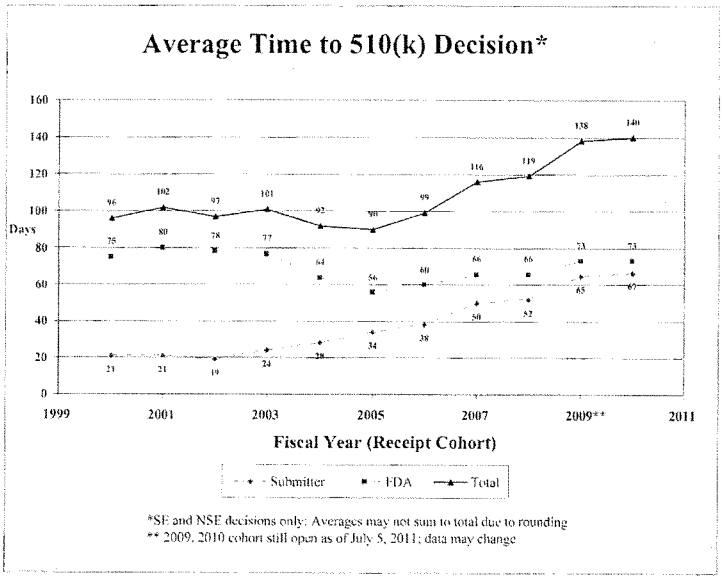
regulations on employment, innovation, and economic growth. For example, the Unfunded Mandates Reform Act of 1995 requires that major rules include estimated effects on employment, competitiveness, and growth. Executive Order 12866, Regulatory Planning and Review, requires all federal agencies to consider effects on innovation when writing regulations.

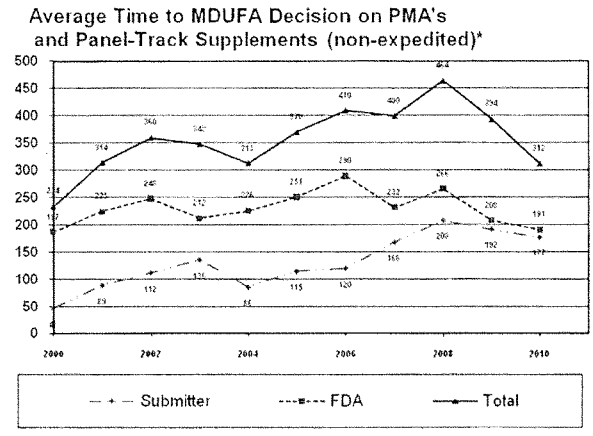
In addition, agencies periodically conduct reviews of existing regulations pursuant to a variety of authorities, changes in the law, or other circumstances. For example, the Regulatory Flexibility Act requires agencies to conduct reviews within 10 years of regulations that have a significant economic impact on a substantial number of small businesses. And, under 21 CFR 10.25(a) and 10.30, FDA may review a regulation if a person submits a petition asking the Commissioner to issue, amend, or revoke a regulation.

In this spirit of openness and transparency, in 2010, CDRH initiated its own review of its process for premarket review of medical devices and undertook two significant initiatives to improve the Agency's medical device premarket review programs.

It's important to note that, in terms of performance, FDA has been consistently strong, meeting or exceeding goals agreed to by FDA and industry under the Medical Device User Fee Amendments (MDUFA) for approximately 95 percent of the submissions we review each year. FDA consistently completes at least 90 percent of 510(k) reviews within 90 days or less. In the limited areas, where FDA is not yet meeting its MDUFA goals, the Agency's performance has been steadily improving, despite growing device complexity and an increased workload, without a commensurate increase in user fees.

MDUFA metrics reflect FDA time only; they do not reflect the time required for industry to respond to requests for additional information. As the graphs below illustrate, while the time FDA spends reviewing an application has improved for both low- and high-risk devices, overall time to decision—the time that FDA has the application, plus the time the manufacturer spends answering any questions FDA may have —has increased. FDA bears some responsibility for the increase in approval times and has been instituting management changes. As a result, in 2010, total time for 510(k)s appears to have stabilized and preliminary data suggest that the total time for PMA decisions is improving.





*Times may not add to total due to rounding
** 2009, 2010 cohort still open as of July 5, 2011; data may

Industry also bears some responsibility for the increase in overall time to decision, which I discuss in detail on page 15 of my testimony.

The 510(k) Action Plan

FDA recognizes that concerns have been raised about how well CDRH's premarket review program is meeting its two goals of ensuring that medical devices are safe and effective and fostering medical device innovation. Some stakeholders—particularly in industry—have argued that a lack of predictability, consistency, and transparency in the 510(k) program is stifling medical device innovation in the United States and driving companies (and jobs) overseas. Other groups, including health care professional, patient, and third-party payer organizations, have argued that the 510(k) program allows devices to enter the market without sufficient

evidence of safety and effectiveness, thereby putting patients at unnecessary risk and failing to provide practitioners with the necessary information to make well-informed treatment and diagnostic decisions.

In response to these concerns—and because FDA is continually looking for ways to improve its performance in helping to bring safe and effective devices to market—the Agency conducted an assessment of the 510(k) review program and an assessment of how it uses science in regulatory decision-making, which addressed aspects of its other premarket review programs.

The two reports we released publicly in August 2010, with our analyses and recommendations, showed that we have not done as good a job managing our premarket review programs as we should and that we needed to take several critical actions to improve the predictability, consistency, and transparency of these programs.

For example, we have new reviewers who need better training. We need to improve management oversight and standard operating procedures. We need to provide greater clarity for our staff and for industry through guidance about key parts of our premarket review and clinical trial programs and how we make benefit-risk determinations. We need to provide greater clarity for industry through guidance and greater interactions about what we need from them to facilitate more efficient, predictable reviews. We need to make greater use of outside experts who understand cutting-edge technologies. And we need to find the means to handle the ever-increasing workload and reduce staff and manager turnover, which is almost double that of the FDA's drugs and biologics centers.

The Agency solicited public comment on the recommendations identified in the studies and received a range of perspectives from stakeholders throughout the process at two public meetings and three town hall meetings, through three open public dockets and via many meetings with stakeholders. Seventy-six (76) comments were submitted from medical device companies, industry representatives, venture capitalists, health care professional organizations, third-party payers, patient and consumer advocacy groups, foreign regulatory bodies, and others.

After considering the public input, in January 2011, FDA announced 25 specific actions that the Agency will take this year to improve the predictability, consistency, and transparency of our premarket review programs. Since then, FDA has announced additional efforts, including actions to improve its program for clinical trials and Investigational Device Exemptions (IDEs) program. These are based on an analysis of this program that the Agency committed to, as part of its January 2011 announcement.

These actions, many of which were supported by industry, include:

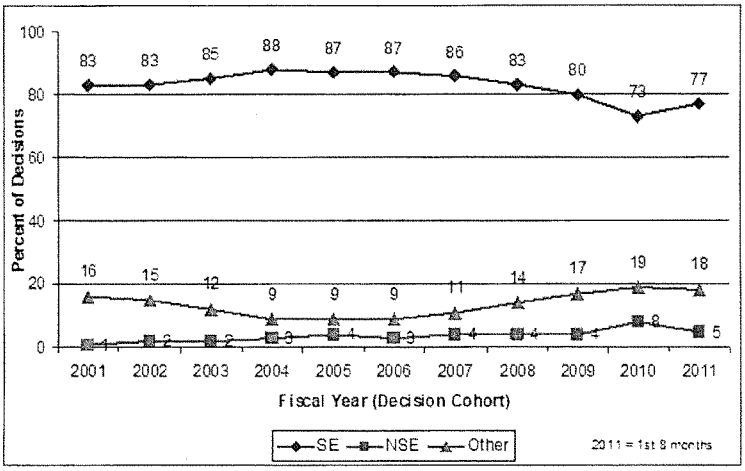
- Developing a range of updated and new guidances to clarify CDRH requirements for timely and consistent product review, including device-specific guidance in several areas such as mobile applications and artificial pancreas systems (to be completed by the end of 2011);
- Revamping the guidance development process through a new tracking system and core staff to oversee the timely drafting and clearance of documents (to be completed by the end of 2011);

- Improving communication between FDA and industry through enhancements to interactive review (some of these enhancements will be in place by the end of 2011);
- Streamlining the *de novo* review process, to provide a more efficient pathway to market for novel devices that are low to moderate risk. This new structure will be described in draft guidance for industry that is expected to be available for public comment by September 30, 2011;
- Streamlining the clinical trial and IDE processes by providing industry with specific guidance on how to improve the quality and performance of clinical trials. (IDEs are required before device testing in humans may begin, and they ensure that the rights of human subjects are protected while gathering data on the safety and efficacy of medical products.) We are also developing guidance to clarify the criteria for approving clinical trials, and criteria for when a first-in-human study can be conducted earlier during device development (to be issued by October 31, 2011);
- Establishment of an internal Center Science Council to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decision-making (already completed);
- Creating a network of experts to help the Center resolve complex scientific issues, which will ultimately result in more timely reviews. This network will be especially helpful as FDA confronts new technologies;
- Instituting a mandatory Reviewer Certification Program for new reviewers (to be completed by September 2011); and,
- Instituting a pilot Experiential Learning Program to provide review staff with real-world training experiences as they participate in visits to manufacturers, research and health care facilities, and academia (to begin in early 2012).

Consistent with the improvements we are making to the program, we are seeing a positive trend in the percent of 510(k) decisions that are "not substantially equivalent" (NSE). For manufacturers, an NSE determination often represents an inefficient use of time and resources. For FDA, NSE determinations require significant Agency resources and time, yet fail to result in the marketing of a new product. The following chart shows an upward trend, until mid-2010, in the percentage of 510(k) decisions that were "not substantially equivalent" (NSE). The most common reasons that 510(k) submissions result in NSE determinations are: lack of a suitable predicate device; intended use of the new device is not the same as the intended use of the predicate; technological characteristics are different from those of the predicate and raise new questions of safety and effectiveness; and/or performance data failed to demonstrate that the device is as safe and effective as the predicate. The vast majority of NSE decisions are due to the absence of adequate performance data, sometimes despite repeated FDA requests.

I'm pleased to report that, consistent with our many improvements to the 510(k) program, this long-standing trend is turning around. From a peak of 8 percent in 2010, the NSE rate has decreased to 5 percent through the first eight months of 2011.

Percent of 510(k) Submissions with an NSE Decision per Year

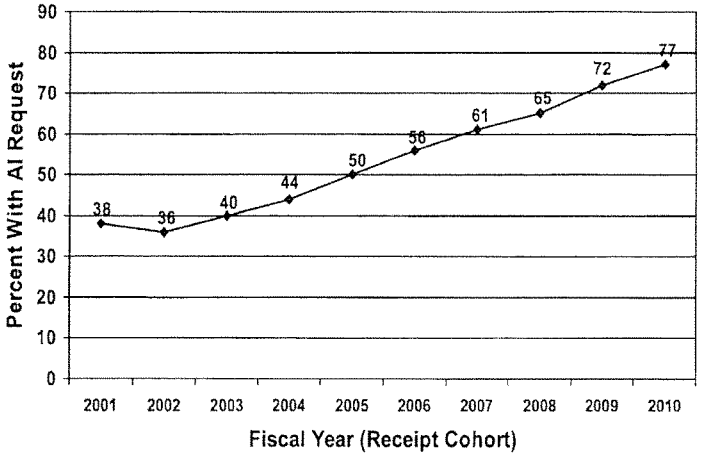


In addition, we need to ensure that industry meets its responsibility to provide us with appropriate data. Poor quality submissions are significant contributors to delays in premarket reviews; these include submissions that do not adhere to current guidance documents, that contain inadequate clinical data (e.g., missing data, or data that fail to meet endpoints), or that deviate from the study protocol agreed upon.

The following chart shows the steep and prolonged increase, since FY 2002, in the percentage of 510(k) submissions requiring an Additional Information (AI) letter after the first review cycle. The increasing number of AI letters has contributed to the increasing total time from submission to decision. In over 80 percent of cases, the AI letter was sent because of problems with the quality of the submission. Examples of submission quality problems that result in the increasing rate of AI letters include: inadequate device descriptions; discrepancies throughout the

submission, e.g., between the indications for use and labeling materials; problems with the proposed indications for use; completely missing performance testing data; completely missing clinical data; and failure to follow the applicable guidance document without explanation. These submission quality problems waste FDA and sponsor time and resources and divert FDA resources from pending, higher-quality applications.

Percent of 510(k) Submissions with an AI Letter in First Review Cycle per Year



We are pleased that, in response to FDA calls for improving the quality of premarket submissions, AdvaMed has improved and made more available training courses for its companies to help them develop 510(k) and PMA submissions that meet FDA standards.

Innovation Initiative

Facilitating medical device innovation is a top priority for FDA. As part of its 2010 and 2011 Strategic Plans, FDA's medical device center has set goals to proactively facilitate innovation to address unmet public health needs. FDA's Innovation Initiative seeks to accelerate the development and regulatory evaluation of innovative medical devices, strengthen the nation's research infrastructure for developing breakthrough technologies, and advance quality regulatory science. As part of this initiative, CDRH proposed additional actions to encourage innovation, streamline regulatory and scientific device evaluation, and expedite the delivery of novel, important, safe and effective innovative medical devices to patients, including:

- Establishing the Innovation Pathway, a priority review program to expedite development, assessment, and review of important technologies;

- Issuing guidance on leveraging clinical studies conducted outside the United States;

- Advancing regulatory science through public-private partnerships;

- Facilitating the creation of a publicly available core curriculum for medical device development and testing to train the next generation of innovators; and

- Engaging in formal horizon scanning—the systematic monitoring of medical literature and scientific funding to predict where technology is heading, in order to prepare for and respond to transformative, innovative technologies and scientific breakthroughs.

A public docket has been set up to solicit public comment on the Innovation Initiative proposals, and a public meeting on the topic took place on March 15, 2011. In the near future, FDA will announce actions it plans to take under the Initiative.

The Role of Regulation in Patient Safety

As we continue to look for ways to improve our ability to facilitate innovation and to speed safe and effective products to patients, we must not lose sight of the benefits of smart regulation, to the industry, patients, and society. Medical device regulation results in better, safer, more effective treatments and world-wide confidence in, and adoption of, the devices that industry produces.

We at FDA see daily the kinds of problems that occur with medical devices that are poorly designed or manufactured, difficult to use, and/or insufficiently tested. For example, we received an IDE, or request to initiate a clinical trial, for the PleuraSeal Lung Sealant System, which was indicated to prevent Persistent Air Leaks (PALs) resulting from lung surgery. The IDE was designed to test whether the device would help to seal an incision in the lung better than the standard of care—i.e., stitches—alone. The company began marketing the device outside the United States for prevention of PALs in November 2007, and then began its clinical study to support approval in the United States. Midway through the study, it was apparent that three times more patients who received PleuraSeal had poor outcomes (PALs) as compared to patients whose incisions were closed using standard techniques. This showed that PleuraSeal was not effective in preventing PALs after lung surgery. Subsequent to discovering these results, the manufacturer announced a worldwide recall of all PleuraSeal lung sealant systems. PleuraSeal

was removed from the market in the EU and the IDE was withdrawn. This device was never approved in the U.S.

As another example, an abdominal aortic aneurysm (AAA) is caused by a weakened area in the aorta, the main blood vessel that supplies blood from the heart to the rest of the body. When blood flows through the aorta, the pressure of the blood against the weakened wall causes it to bulge like a balloon.

FDA received the first IDE, or request for approval of a clinical trial, for an AAA stent graft in 1994. Premarket problems were identified during clinical testing related to delivery and deployment, stability of fixation and structural integrity of these devices. As result of the findings of the studies, FDA required study suspension, redesign, or initiation of new studies for nine AAA stent grafts.

AAA Stent Grafts were marketed in Europe as early as 1997, and were put on the market there without the support of clinical studies as is required in the U.S. Postmarket reports identified serious problems with the devices on the EU market, including late rupture of the aneurysm, persistent leaks, continued AAA enlargement, graft obstruction, fracture, migration and kinking. Six devices have been permanently discontinued in the EU due to complications, and three were redesigned and reintroduced.

The Aptus AAA stent graft incorporated an innovative staple technology that prevented the graft from migrating following implantation. However, patients developed blood clots in their arms and legs after enrollment in a U.S.-based pivotal clinical trial in February 2009. The problems

were not predicted by preclinical testing. The Aptus AAA stent graft is approved in the EU and is not approved for marketing in the United States.

There are currently six AAA Stent Grafts on the U.S. market. None has been withdrawn from the U.S. market due to these failures.

Outside the United States, pressure is growing toward greater premarket scrutiny of medical devices. A recent report[4] concluded that "For innovative high-risk devices the future EU Device Directive should move away from requiring clinical safety and "performance" data only to also require pre-market data that demonstrate "clinical efficacy," and "The device industry should be made aware of the growing importance of generating clinical evidence and the specific expertise this requires."

The European Society of Cardiology (ESC) recently issued a "case for reform" of the European medical device regulatory system and their recommendations included creating a unified system, stronger clinical data requirements, and more accountability for notified bodies.[5] The ESC cites examples of many different cardiovascular technologies that were implanted in patients in the EU that were then proven to be unsafe and/or ineffective through clinical trials required under the U.S. system and removed from the European market. A recent article in the British Medical Journal discusses the opacity of the European medical device regulatory system, with regard to access to decisions regarding device clearances.[6] The article cites the FDA system's

[4] Belgian Health Care Knowledge Centre. "The Pre-market Clinical Evaluation of Innovative High-risk Medical Devices," KCE Reports 158 (2011) at p. vii, available at *http://www.kce.fgov.be/index_en.aspx?SGREF=20267.*
[5] See "Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform," Fraser, et al., *European Heart Journal*, May 2011.
[6] See "Medical-device recalls in the UK and the device-regulation process: retrospective review of safety notices and alerts." Heneghan, et al., *British Medical Journal*, May 2011.

transparency as helping physicians to make informed decisions on which devices to use and giving patients access to information on devices that will be used on them.

Additionally, a report released by the Belgian Health Care Knowledge Centre[7] calls upon the European Commission to implement reforms to make the EU review process for high-risk devices more like that of the United States.

CONCLUSION

Mr. Chairman and Members of the Subcommittee, I share your goal of smart, streamlined regulatory programs. The Department's plan for regulatory reform under President Obama's Executive Order will heighten and maintain the focus on this important principle. Thank you, for your commitment to the mission of FDA, and the continued success of our medical device program, which helps get safe and effective technology to patients and practitioners on a daily basis. I am happy to answer questions you may have.

[7] See "The pre-market clinical evaluation of innovative high-risk medical devices," KCE reports 158C. Belgian Health Care Knowledge Centre. 2011.

Mr. STEARNS. I thank you, Dr. Shuren.

Just so there is no lingering uncertainty with respect to Medtronic Sprint Fidelis approval that was discussed on the first panel, I think you were here to listen to that, was the Medtronic device at issue approved as a 510(k) as Dr. Curfman stated in his testimony?

Mr. SHUREN. No.

Mr. STEARNS. Well, then that and other factual inaccuracies that also included in Dr. Redberg's letter to Ranking Member Waxman, which is attached to the Democrats' supplemental memo, throws into serious doubt Dr. Curfman's and Dr. Redberg's conclusions. I ask the gentlelady, does the minority still wish to include that supplemental memo in the record?

Ms. DEGETTE. Yes, it has already been included.

Mr. STEARNS. OK. We just wanted to establish that.

Dr. Shuren, you have been at the FDA not just the 2 years in this present position, how many years were you before that?

Mr. SHUREN. I first started in 1998 but I also worked over at the Medicare program, and I came back in 2003 and had been there since then.

Mr. STEARNS. So that is 8 years from 2003, and before that how many years were you there?

Mr. SHUREN. About——

Mr. STEARNS. Two?

Mr. SHUREN. Approximately two.

Mr. STEARNS. So our records show you actually have been there 10 years. Would that be a fair statement?

Mr. SHUREN. That would be a fair statement.

Mr. STEARNS. OK. And I think in your opening statement here, you say that the FDA needs to take steps to improve predictability, consistency and transparency. So the question is, since you have been there 2 years, I guess rhetorical, why hasn't all that been done, and maybe more specifically, your comment that FDA needs to improve management oversight and standard operating procedures, and I guess the question is, since you have been there for 2 years have you done that?

Mr. SHUREN. So the answer is yes, we have actually already started to make improvements. When I first came in, there were a lot of questions from different sides about were the programs not working well, were we too risk-averse. Others were saying we are too risk-permissive. And what we said we needed to do is a thorough assessment of the programs first, understand the problems, identify the root causes, and then determine the appropriate solutions. That is what we spent much of 2010 doing. We went around the county to hear from different people, not just asking people to come to us but our going out to them, and that is what is contained in our two reports. We put out the recommendations of what we would do, and we wanted to get public input first to make sure we were doing what was right before we proceeded, and in fact, we had heard from industry and even some in Congress, please don't rush into making changes, we want to make sure you finish your process first.

So we did that, but we moved quickly so that we could wrap up and start putting improvements in place, and one of them already

set up is the center science council that I mentioned. This is a body of our senior managers and experienced scientists, and to them are brought some of the important issues to be decided by the center. For example, where in the past a decision to——

Mr. STEARNS. Would it be fair to say what you are talking about is what you intend to do?

Mr. SHUREN. No, no, no. The center science council is already set up.

Mr. STEARNS. OK. Let us say all the things you said are good things. You heard Dr. Fischell, didn't you, in which he said the "FDA's device center over the past few years is the worst I have experienced in 42 years," so then I asked him to narrow it down, is it 4 years ago, 5 years ago, the last 2 years. He indicated, as you heard, it is really under your watch. Isn't that what you heard from him?

Mr. SHUREN. That is what I heard from him but——

Mr. STEARNS. So we both agree, that is what he said. So under your watch, here is a very competent inventor of the United States award 200 patents in Europe and the United States, he said it is the worst experience he has seen in 2 years. Do you agree with him?

Mr. SHUREN. No, I don't think we are the worst in terms of running the center. I do think in terms of performance, we have seen performance worsen.

Mr. STEARNS. So performance has worsened in the last 2 years?

Mr. SHUREN. No, it has but it started before then. If I could show, actually I can show you the data if you would like to see it. First off, if you would just go to chart number 4.

Mr. STEARNS. So he is saying in his opinion, it is worse. You are saying in a sense that it has been bad but it is not the worst.

Mr. SHUREN. Well, what I——

Mr. STEARNS. Would you agree the last 2 years are bad?

Mr. SHUREN. What I would like to explain is that performance has gotten—I think some things are actually now starting to improve. For example, if you look at the chart here, this is for 510(k)s. When we have deficient applications or we have questions, we send out what is called an additional information letter. If you look at the chart here, the percent of 510(k)s that we are sending letters out on actually started to increase in 2002. If you next put up the chart for number two, you actually see our performance on 510(k)s over time, and what I want to lay out for you is that there have been issues here going on many years that have been increasing.

So what you will see on the chart here is our average time for a decision. The top line is what we call total time. This is the time it takes FDA and the time it takes industry. The middle line is FDA's performance. The bottom line is industry time. What you will see here is that starting in 2005, total time is going up. In fact, if you overlaid even our first chart, which you don't have to do, but from 2002 recall those letters going up. Now watch industry time going up and then followed after it while our performance started to improve, total time goes up. If you look at the very end and the numbers at the end are not done yet, the applications we are looking at the very end shows 2010.

Mr. STEARNS. So in your opinion, things are changing? That is what you are arguing?

Mr. SHUREN. That is what I am trying to say. Things are starting to change. We have a long way to go.

Mr. STEARNS. Long way to go, but you do admit that the last 2 years have been not as, shall we say, competent and——

Mr. SHUREN. No, I wouldn't say that. I think for some indicators in terms of times, those numbers——

Mr. STEARNS. Let me get to this quote here. Is FDA Commissioner Hamburg your boss?

Mr. SHUREN. Yes.

Mr. STEARNS. You have said that the level of criticism the device center has received has only compounded the problem. FDA Commissioner Hamburg, however, acknowledged last week that "much of the criticism was deserved." Has Commissioner Hamburg expressed this concern to you? Yes or no.

Mr. SHUREN. Yes.

Mr. STEARNS. If so, when did she give you that criticism to you?

Mr. SHUREN. For over the past year, we have been aware of——

Mr. STEARNS. So she has criticized for the last year to you. Is that correct?

Mr. SHUREN. What she is conveying is the criticism she has heard from others and that she and I both agree with, that many of the concerns raised are accurate.

Mr. STEARNS. Did she specifically tell you to do something about it after she gave this criticism to you?

Mr. SHUREN. I started to do something about it from the day I hit the center. I had heard of these and known about the problems before I ever took on my job, and one of the very first things I did when I started was to announce, we need to look at this. In fact, when I first started the job, I was acting. I didn't know I would be permanent, and I told the commissioner, look, if you are going to give me this job, I am not going to be here and just be a guardian, there are things we need to do and this is one of the things we need to do, we need to get to the bottom of what the problems are, and I asked permission to do that and was told yes, you can proceed——

Mr. STEARNS. I think my only concluding comment is that from our perspective, it looks like you are on the go right now but you weren't necessarily on the go 2 years ago, and we have this lag of which Dr. Fischell has talked about and which a lot of our people in the first panel just complained about, and so you heard them. So my time is expired.

The gentlelady from Colorado is recognized for 5 minutes.

Ms. DEGETTE. Dr. Shuren, thank you very much, from my perspective, for your patience today with the very, very long day we have had. In my short time, I have a lot of ground to cover so I want to try to keep this flowing as much as possible.

It looks to me from the two charts that you put up that the number of device applications is increasing. Is that correct?

Mr. SHUREN. The number of device applications has been increasing. In fact, since 2004, it has increased through 2010 about 26 percent.

Ms. DEGETTE. And has the staff in your division of the FDA increased to keep pace with that?

Mr. SHUREN. It hasn't kept pace with the increase in our workload. If you look from 2007 to 2010, and actually we have a chart, number six, it will show the increase in workload is about 27 percent but we have not had the staff increase for premarket review to handle all that work.

Ms. DEGETTE. And that is even including the user fees or the PDUFA fees that are coming up, right?

Mr. SHUREN. That is correct.

Ms. DEGETTE. OK. Now, you said that the 510(k) letters are going up. Why is that? Is that because of insufficient applications or the increase in applications, or both?

Mr. SHUREN. So we did an analysis of the letters we sent out in 2010. We looked at about 100 of them and then we looked at follow-up letters if the manufacturer didn't respond to all of the deficiencies. The causes for those letters are multifactorial. In some cases, it is our fault. We found that 8 percent of the time when we sent out letters, we asked for——

Ms. DEGETTE. I don't mean to stop you, so there are a lot of reasons why the number of letters are going up?

Mr. SHUREN. Sometimes we ask for things we shouldn't. Other times companies didn't provide information they knew they should have provided.

Ms. DEGETTE. OK. Now, you heard me say, and you knew this, I am the chair of the Diabetes Caucus, and I know that you are aware of the guidance that the FDA is working on towards artificial pancreas and also towards these low-glucose suspending systems that Ms. Sagan was talking about. Are you familiar with that?

Mr. SHUREN. Yes, I am.

Ms. DEGETTE. Is the agency still on target to have the guidance on the artificial pancreas approved by December?

Mr. SHUREN. Yes.

Ms. DEGETTE. And can you tell me how the agency is going to be working with the manufacturers of both the artificial pancreas and also the pump and glucose monitor combinations on both of these systems, the artificial pancreas and the low-glucose suspend systems? How are you going to be working with manufacturers so we can move these issues along?

Mr. SHUREN. So we allow for meetings with the companies before they are even at a point to actually——

Ms. DEGETTE. Is that happening?

Mr. SHUREN. Yes.

Ms. DEGETTE. OK.

Mr. SHUREN. We do meet with companies, and when we actually deal with the clinical trial, we have set out for an interactive review so there is a rapid turnaround. In fact, one company right now, I just got told by the head of my artificial pancreas group, he has spoken with the company five times this week.

Ms. DEGETTE. OK. Good. So you feel like we are on track with all of those systems. Because that is important to a lot of us.

Now, beyond diabetes devices, I want to ask you more generally, because all of us on this committee on both sides of the aisle are

concerned. You know, you heard the first panel, we are concerned about all these devices. What other actions is the FDA taking to improve device review and safety?

Mr. SHUREN. So to get the program back on track, we need to have clearer policies. We need to put clarification of what companies need to do and our expectations. We need to train our people and to have training to industry. We need to have the procedures in place in our center to make sure that the decisions are made at the right level so that we make the right call.

Ms. DEGETTE. And do you think that your staff has sufficient training or could they need more?

Mr. SHUREN. Oh, they do need more.

Ms. DEGETTE. And is that going to require adequate funding?

Mr. SHUREN. We will need to have sufficient funding, not just to have the training but for the people to take the time from not doing premarket review so that they can go off and do the training, and one of the challenges when you have limited capacity in your staff is that they have to pick and choose between do I do the training but it is going to take longer on the premarket review and we would like to have sufficient number of staff to do the work and ensure people can do the training and ensure that they can develop the guidance documents which are so helpful to industry.

Ms. DEGETTE. Now, you heard Dr. Fischell's idea on the first panel of just having peer review by people in the field like putting three people on. What is the FDA's position on that?

Mr. SHUREN. I think the FDA still has responsibility to review those applications but we need to make far better use of outside experts, which is why we are setting up four of these networks of experts so we can go out to people who understand the new technology, experts in the field, and try to answer important scientific questions. We will never and can never and should not expect to have all the expertise in house but we need to have sufficient expertise in-house so we can reach outside and have the right kind of conversations to learn from those outside experts. I am a neurologist. I can talk to another neurologist. You are not going to send me out to talk to an orthopedist

Ms. DEGETTE. OK. Thank you, Doctor.

Mr. STEARNS. Dr. Burgess is recognized for 5 minutes.

Mr. BURGESS. Submit for the record that no one can talk to an orthopedist.

Mr. SHUREN. My brother is an orthopedist, and I agree with you.

Mr. BURGESS. Dr. Shuren, you have been very good to speak to me several occasions about some of these problems, and we have talked about some of the issues regarding the FDA's regulation, your regulation of laboratory-developed tests. Of course, we already have the CLIA structure in place that does that regulation currently. If we are going to talk about improved safety standards, about thousands of new tests and many more coming down the pipeline, how do you propose that FDA, if it going to take on this task and take it away from CLIA, how do you propose to be able to do that with all the other stuff that you have got to do?

Mr. SHUREN. Well, first off, CLIA doesn't get to the oversight of the tests, it gets more to the quality of the laboratory and the ability of a laboratory to perform those tests, whereas the FDA handles

the safety and effectiveness of the tests. We have been looking at how could we handle that workload if it were to come in, and that is why any policy we would put out would be phased in over time to try to address incoming workload. Secondly, we would be looking at leveraging our third-party review program we already have to help on reviewing some of the lower-risk devices, and in addition, we look at some of the tests to say with experience, maybe we don't need to look at them premarket, we can down-classify them, and in fact, just the other week, we down-classified 30 devices that we no longer will be asking for premarket review on.

Mr. BURGESS. I appreciate you being here while we heard the testimony from all the panelists because I do think it was important that you hear that. I mean, this is the type of thing that we hear in our offices or I hear in my office week in and week out—we have got this thing, we have got this stuff, we have got this test and it has been in the pipeline for 3 years, 5 years, 17 years and we are no closer today than we were when we started. So I think it was important that you heard and felt some of that frustration. And you and I have talked about some of these things specifically in the past. At some point I would like to know what we have done at the FDA to improve that process, but can you give us any idea of the volume of work that is there bottled up at the FDA right now?

Mr. SHUREN. Well——

Mr. BURGESS. If you put everybody at every desk and said no holidays, you don't even get to go home at night until all this work is finished, would you be able to get that done?

Mr. SHUREN. No. Actually——

Mr. BURGESS. Since the trial lawyer next to me brought it up, if this were a plaintiff's firm and this were a product liability suit or a class action suit, they would have no trouble sifting through a whole basement full of data, digitizing it and getting it available to their attorneys in a relatively short period of time. They would hire enough people to get that done because it would be important to them, and what it suggests to me is, this is not important to the FDA.

Mr. SHUREN. No, it is important to us, and if I had the ability to hire more people, I would do so. And we can push our people, I can chain my people to their desks 24/7, but it is not like I have one case before me. I have a growing workload and it doesn't go away.

Mr. BURGESS. Now, Mr. Waxman brought up the issue of funding but it looks like from the information that we have with the user fee tax that it out there that your funding has significantly increased over time. So Dr. Sharfstein said he had plenty of money when I asked him that question a year ago. Are you telling us differently today?

Mr. SHUREN. I think—and I am very happy to go back to the record. I think what Dr. Sharfstein was saying is that resources along was not enough to handle it, and I think it was the context of globalization, but we do need adequate resources, but let me be clear. Resources are not the only thing at issue. There are a lot of things at the center that need to be fixed. We know what the problems are, we know what to do, and we are on it. We are already

making changes. There are some things we have to work with with industry on. We need to get the data that they are supposed to send to us, and we are already in discussions with industry about that. In fact——

Mr. BURGESS. I am going to have to interrupt you because I am going to run out of time, but I don't think there is any question the device times have significantly increased, the approval times have significantly increased. I am glad to hear you say it is not just solely due to funding, but we have to improve.

Now, Michael Mandel was here on our panel earlier. He was from the Progressive Policy Institute, and he had a story to tell about this MelaFind, and do you think that the FDA was impeding the implementation of being able to use this device that he was describing?

Mr. SHUREN. I think in the case, there were issues with the data that was sent to us. What we are doing now is going through the data provided, and keep in mind, the manufacturer then more recently a few months ago changed the indication they were looking for. We are trying to see, does the data support what the manufacturer would like to do or something close to it, and if so, then we would approve that device.

Mr. BURGESS. But the fact remains that it has taken so long, and the rules seem to be changing. Is the FDA causing us to lose our edge in the development of these new devices?

Mr. SHUREN. I think the FDA needs to do a better job to ensure that we keep our edge as the world's leader in medical device innovation.

Mr. BURGESS. Thank you, Mr. Chairman. I will yield back.

Mr. STEARNS. He asked you, do you think we are losing our edge. Just yes or no.

Mr. SHUREN. I don't think we have lost our edge. I think if there are steps we don't take, we are at risk for losing it in the future.

Mr. STEARNS. Thank you. And the gentleman from California, Mr. Waxman, is recognized for 5 minutes.

Mr. WAXMAN. Thank you very much.

Dr. Shuren, I want to ask you about a statement that Advanced Medical Technology Association, known as AdvaMed, the medical device industry trade association, issued today. I would like to ask that this statement be made part of the hearing record, Mr. Chairman.

AdvaMed is the leading device industry trade group. According to their Web site, their members produce 90 percent of the medical devices sold in the United States. Here is what AdvaMed had to say: "The medical technology industry has long recognized that a strong and well-functioning FDA is vital to maintaining America's preeminence in the medical technology innovation and we support the current regulatory framework in the United States." Do you have any reaction to this statement?

Mr. SHUREN. I am glad to hear it. Actually, recently I was in a meeting with senior officials from AdvaMed and they had said to me that they support the current approval and clearance standards for the United States.

Mr. WAXMAN. Well, their press release says that "we believe that any steps necessary to address the situation can be taken without

changing the current robust statutory standards for clearance and approval of medical devices." Earlier today, we were hearing from member after member on the Republican side insisting that the FDA and the regulatory standards required by the agency for device approval are destroying innovation and causing device manufacturers to move overseas. But the leading device manufacturer trade group puts out a press release that says the best way to maintain America's preeminence in this area is, and I quote, "a strong and well-functioning FDA requiring industry to comply with robust statutory standards for clearance." Now, I assume they don't want the statutory requirements changed, but when they talk about a robust FDA, I am sure they are talking about a well-funded one.

I must take exception to the comment that was made if FDA really cared, they would hire more people. You are hiring as many people, I presume, as you can afford. Isn't that correct?

Mr. SHUREN. That is correct, and we also suffer from a high turnover rate, which makes it so much harder to try to keep up with our losses.

Mr. WAXMAN. Well, if the Republican budget as proposed passes, it would provide a 10 percent cut over $200 million in the FDA budgets. Cut of this magnitude would affect every facet of FDA operations. You have a tough job to do, balancing the desire of manufacturers and patients to get quick approval for devices with your statutory requirements to make sure they are safe and effective. I think this is shortsighted to make these kind of budget cuts. Do you differ with me on that?

Mr. SHUREN. I am deeply concerned that budget cuts would cause us to not only lose people but our performance will worsen, and that will not be in the best interest of industry, it won't be in the best interest of patients.

Mr. WAXMAN. Do you have difficulty attracting the best people?

Mr. SHUREN. We do have a challenge attracting the best people. The circumstances are, it is a high workload for people. People get burned out. And the pay for our people, particularly our frontline managers, doesn't compare to what they get in industry. In fact, in some respects, it is not necessarily even the same for other parts in the agency and so we have a very high turnover rate.

Mr. WAXMAN. So you have a high turnover rate, you have got a difficult balancing job to do. You recognize other internal problems that you are trying to deal with in the medical device area in terms of, I will say it, culture or inability to move as quickly as we would hope they would, and you are trying to address those issues?

Mr. SHUREN. I am. And in fact, these same problems were seen in the drug program 10 years ago, same thing in PDUFA where they had high turnover rate, there were concerns about slow review times, and the drug program was able to get on top of it. I think people may have heard Dr. Woodcock the other week testify, talk about how now they are so much faster than Europe and there was a health affairs article out about it recently and what made it, they had to make some internal changes but ultimately the drug industry got behind the program. They provided additional funding and that program took off. In fact, right now the drug program, and I am not saying it should be the same size but it is three times the

size of the device program. They have five times as many medical officers. They get 10 times the amount in user fees, and in fact, 60 percent of their larger program is supporter by user fees whereas 20 percent of my smaller program is supported by user fees, and that ultimately made a big difference in being successful. I hope ultimately our program is much more successful like the drug program.

Mr. WAXMAN. Well, we hope so too, and I hope this hearing will lead to a very constructive approach by a Congress that has not very well performed so far this year. We have done practically nothing. We may not even raise the debt ceiling and allow our economy to go over the cliff, and we are telling you how to run an agency, but I hope as we do our job and improve in our job performance that we can help you, not cause more problems for you.

I see my time is expired and I yield back, Mr. Chairman.

Mr. STEARNS. The gentleman's time has expired. The gentleman from Nebraska is recognized for 5 minutes.

Mr. TERRY. Thank you, Dr. Shuren, and I appreciate that you have outlined some of the areas that you have identified as needing improvement, so I appreciate that you are willing to do that. Lisa Jackson is much more fun that you are, frankly, up here. At least she fights with us instead of coming and recognizing that there are issues and problems that need fixing.

Mr. SHUREN. I save it for my wife.

Mr. TERRY. We share something.

But on the money part, let us start with that, and then I want to tag along on what Diana was talking about with some of the artificial pancreas and how we can work through it maybe even faster, but as I understand from a Congressional Research Service report, funding from 2008 to 2010 increased 35 percent for the medical device review process. So it has gone from in 2008 $275 million to $368 million. So I find it hard to really grasp that the 2-year period that we are talking about, funding was increased, delays increased, problems occurred and it is all related to the lack of money. So my question to you is, the 2 years you have served there, there has been an increased of dollars, you have had a turnover. Is the turnover related to pay?

Mr. SHUREN. Turnover is related to pay and to workload. I will say in terms of the funding we got—and I haven't seen that report to look at percentages—but we did get increased appropriations from Congress. Congress also tells us how that money should be used, and that money predominantly was directed towards postmarket safety and globalization, some science. We really didn't get the big boost for premarket review. We did get an increase in user fees, which we focused on premarket review, and if you are talking about the years 2008 to 2010, the enacted user fees that we can get in 2008 were for my center, $26.6 million, and they went up to $32.8 million in 2010. So between those two years, I had about an increase in $6 million in user fees, enacted user fees, and those while I have been on the job, and recall, I came in in late 2009, so I am dealing with money coming in for 2010, I tried to direct more money to premarket review. Twenty eleven was a bit of a challenge because, as you know, I understand the challenges you all go through.

Mr. TERRY. Oh, that is right. We did pass a budget, didn't we? It is the Senate that hasn't.

Let me get to the low-glucose suspend systems and artificial pancreas. Do you know how long those have been before the FDA medical devices for approval?

Mr. SHUREN. Well, there is no true artificial pancreas. No one has developed it. There is nothing commercial. The low-glucose suspend, the company has come to us, I believe, and this is my understanding from my staff, but I believe it is just been in the past year, and we have been working with them to get up to do the studies they need and ultimately, hopefully if things turn out right, then approve it and have it on the market.

Mr. TERRY. And the process that has been there for a year, what information is required at this stage?

Mr. SHUREN. So at this stage is to show it is safe and effective. The device is available in other countries, but from what we were able to see and particularly in Europe, it wasn't approved for the low-glucose suspend. It has that as a feature but it is not in its indications for use, and then we asked, did you do any of the prospective clinical studies to show that that feature works, and they hadn't. They didn't need to do that for Europe, so that is what we are asking for here in the United States.

Mr. TERRY. All right.

Mr. SHUREN. And I would like to see such a device out there, and I will tell you, the head of my artificial pancreas group, he is a type 1 diabetic. He has said to me, if we have something out there that worked that was safe and effective, he would use it.

Mr. TERRY. In my last 30 seconds, what do we need to do to get this done? You have got the JDRF out here, others that are listening. What is necessary right now?

Mr. SHUREN. So right now, we need to get the next guidance out there. We need to finalize the one we put out on low-glucose suspend. We need to get the next one out on artificial pancreas. That will be out on December 1. In the best of all possible words, I would be able to beef up and have a stronger staff to focus on this. We deal with so many disease disciplines that we don't have enough of the people to do all of that work, and I will tell you in the case of this guidance that we just put out, I actually pulled endocrinologists from my other centers and asked them, would you be willing to give up your time on reviewing drugs and biologics to help us out on this just so we have the capability to get it done as soon as possible.

Mr. TERRY. My time is up.

Mr. STEARNS. The gentleman's time is expired. The gentleman from Michigan, Mr. Dingell, is recognized for 5 minutes.

Mr. DINGELL. Mr. Chairman, I thank you.

Would you please submit us a list of measures you are taking to improve the consistency of the review process, please?

Mr. SHUREN. Yes.

Mr. DINGELL. How many FTEs in your center work on device review?

Mr. SHUREN. The device review process under our user fee program is 949 FTEs as of 2010.

Mr. DINGELL. In your tenure at the center, have you witnessed a high turnover among the review staff? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. What is your turnover rate? Would you submit that for the record, please?

Mr. SHUREN. Yes.

Mr. DINGELL. Amongst the review staff currently employed by FDA, what is their average tenure in that position? Please submit that to the record.

Mr. SHUREN. Yes.

Mr. DINGELL. Now, as I am sure you are well aware, the House recently passed H.R. 2112, the fiscal year '12 agriculture appropriations bill, which would cut the FDA budget by roughly 11 percent, or $285 million. Please submit for the record what is the result of that on your efforts to improve the handling of new permits for the devices that we are talking about. Would you do that, please?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, if the proposed cuts to the FDA budget included in H.R. 2112 are enacted, will FDA have to lay off employees? Yes or no.

Mr. SHUREN. Yes, there is a likelihood we may have to lay off employees.

Mr. DINGELL. How many will have to be laid off? Will you submit that for the record, please?

Mr. SHUREN. Yes.

Mr. DINGELL. And I want that. I don't want it strained through OMB. I want that delivered to this committee.

Now, will the proposed cut jeopardize the number of review staff that FDA is able to employ at the center? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. By what order of magnitude? Submit that for the record, please.

Mr. SHUREN. Yes.

Mr. DINGELL. Will the proposed cut have a detrimental impact on any efforts to improve reviewer training at the center?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, I would note that one of the complaints that my office consistently receives is that medical device approval process has a certain inconsistency from reviewers at the Center for Devices and Radiological Health. Have you taken steps to improve reviewer training? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. Would you please define what those are for the purposes of the record?

Mr. SHUREN. Yes.

Mr. DINGELL. And would you also submit to us, please, what steps you are taking to improve the capability of your reviewers there?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, there are some areas of improvement in the current medical device approval process but I would ask my colleagues here, does anybody remember the Dalkon Shield? Anybody around here? Well, 3 million American women used that device. They were assured it was safe in the early 1970s. Yet the result

was widespread cases of pelvic inflammatory disease, spontaneous abortions, ectopic pregnancies and infertility. I was here when this committee created a medical device law in 1976 at the urging of my good friend, now deceased, President Ford, a Republican.

So is there anybody around here that wants to return to what President Ford called the horse and buggy days of device regulation? Do you want to do that?

Mr. SHUREN. No.

Mr. DINGELL. Now, I want to remind everybody here that first of all, we face huge risks. We talked earlier about pharmaceuticals that kill people and cause children to be born with flippers, but I would like to have you tell us what you have found to be your experience with the money that you have gotten in terms of having your staff financed in good part by the funding of your agreements with industry for paying for the cost of that. Would you submit that for the record, please?

Mr. SHUREN. Yes.

Mr. DINGELL. And I would ask you to just tell us yes or no, are you more able to provide the services that you need to do now that you have that particular program?

Mr. SHUREN. Yes.

Mr. DINGELL. And of course, that is true in the case of pharmaceuticals, is it not?

Mr. SHUREN. Yes.

Mr. DINGELL. Mr. Chairman, I thank you.

Mr. TERRY [presiding]. Thank you, Mr. Dingell.

Mr. Bilbray, you are recognized for 5 minutes.

Mr. BILBRAY. Doctor, the gentleman from California was pointing out that, you know, you could have been facing a 10 percent cut in your budget. Are you aware that venture capital in medical device research is down almost 40 percent? That is about 30 percent more than the reduction of other venture capital in high tech.

Mr. SHUREN. I don't know the actual figure right now for investment.

Mr. BILBRAY. Would you have any explanation of why those investors who traditionally went to research in medical devices would have such a large reduction in proportion to maybe those who are investing in other high-tech devices that don't relate to medical?

Mr. SHUREN. What I can say in terms of what I have been told, and told by industry or industry reports, it is multifactorial. I mean, one is with the global recession, venture capital investment went down across the board, and the VCs have become more risk-averse. They are looking for investing in technologies that are further along in development. At the same time, there are some things on our end.

Mr. BILBRAY. OK. What——

Mr. SHUREN. Insufficient——

Mr. BILBRAY. Go ahead.

Mr. SHUREN. I was going to say, insufficient predictability from FDA is something that can also——

Mr. BILBRAY. Because that is a huge gap, 30 percent between venture capital for an iPhone as opposed to venture capital for a melanoma scanner is a huge gap, and you do say that you think

that the regulatory oversight is one of the major—or a major problem that we need to address with that discrepancy?

Mr. SHUREN. Well, I think having sufficient predictability is an issue we need to address regardless. I mean, when I looked at VC investment, and like I said, it was down, some of the figures from 2010 showed that devices were still the fourth leading area for investment and had held that way, but I do understand from the VCs and I do take this seriously that if we can improve predictability, we can lead to more investment in device technology.

Mr. BILBRAY. OK. Let us talk about a device that was brought up in the testimony and, you know, there is a lot of people that don't want their devices or their items brought up because they are concerned about it affecting their review process, which I think is a concern in itself, but we are not here to talk about that. We are talking about something that was brought up in the first panel, and that is this remote scanner for melanoma. When we are facing a situation with 3 percent annual increase, annual increase on child melanomas, 8,700 people die a year from this, that we have a device that may be practical for a general practitioner to use to detect melanomas that may not be following the regular description, why was that device basically denied the ability to go through a review process, a review panel?

Mr. SHUREN. The decision the first time around not to have the device go to the advisory panel was wrong. The staff made the wrong call. It should have been allowed to go to the advisory panel. It eventually was. It was supported. It was a very slim margin. It was 8–7. We went back——

Mr. BILBRAY. How much of a delay did that put in?

Mr. SHUREN. I don't know.

Mr. BILBRAY. Let me just say this. And I don't blame you. I just blame that—I hope both sides of the aisle understand that some of us that have worked in government long enough understand, there is an inherent problem with bureaucracy, and just accept it. It is just one of those things. There is a problem with capitalism but there is a problem with government bureaucracy, and that is, it is too comfortable to say no. It is too comfortable to show up to the office and go through basically review stuff, and there is not the push or the uncomfortable getting something done that you may get at a different angle, and Doctor, the challenge is, what is the accountability to the people who said no and how long was this delay, and I will say this. If you take how many months, and I will challenge how many months, that this device was slowed down, how many people died during that period in the United States from melanoma that could have been avoided possibly if not just dermatologists but general practitioners had the ability to detect this down the line, and how do we get the bureaucracy to understand, this is not about time and it is not about money, it is about people's lives.

There was a comment made this morning about the delay. Who was the doctor who was over in the corner, Mr. Chairman? Fischell. He made the comment that the delay of a few months is not that big a deal when you consider the life span of a drug or a device, OK? Would you agree with that statement?

Mr. SHUREN. Yes, I do.

Mr. BILBRAY. See, my problem is, the people down the aisle were saying the life span of a device, how about the life span of a patient, and a couple months, 10 months, 12 months delay, when you talk about a 12-month delay, how many? Is there 8,700 people that are not going to be detected in this country because we didn't get a device out to the general practitioners that might have been able to use it? That is the kind of concern I would like you to transfer to your rank and file that every day they say no, every day they say let us study it a little more, that may be the cause of people dying because there are two ways of killing somebody in medicine: improper triage and denying proper triage. And the people that say no are just as liable, but you don't read about it, and I will just close with this.

You don't read about those things, you read about the chairman emeritus talking about a morning sickness medicine in the 1950s that caused birth defects, and we all talk about that. We don't talk about in the 1980s when there was a morning sickness medicine driven off the market and people died because that was driven off. Nobody hears about those people that died from not having access to a product. We only hear about those that die because of inappropriate, and the balance needs to be there, Dr. Shuren.

Mr. SHUREN. And let me say first off from my people, they will actually get more grief for taking too long, being too conservative. We are looking at review times, and quite frankly, if things are moving along quickly, there aren't issues. When they are moving slowly, that is when management is coming back and saying we have a problem, and that is when staff get more grief actually. And in terms——

Mr. TERRY. Thank you.

Dr. Green—Dr. Green? I just assumed.

Mr. GREEN. I am just an old city lawyer.

Mr. TERRY. Juris doctorate, the best kind. Right, Mr. Burgess? The gentleman from Texas, you are recognized for 5 minutes.

Mr. GREEN. Thank you, Mr. Chairman.

First of all, I want to reiterate and associate myself with the comments that our ranking member on the studies and how important the work on the artificial pancreas is, and hopefully the time frame that I am seeing will be met by December, and 245 Members of Congress actually urged the agency to consider the draft guidance, so hopefully we will meet those deadlines.

Dr. Shuren, I note that in testimony at other hearings on the same topic, you stated that delays in the device reviews and declines in FDA performance are due to poor quality submissions from the medical device industry. While I agree with you that not every submission is created equal and there are certainly some variations in quality, I find it hard to believe that the dramatic growth we have seen in review times for both PMA devices and 510(k) devices can be fully explained by the sudden decline of the quality in submissions. What other factors explain the dramatic increase in the review times?

Mr. SHUREN. So I agree, that is not the explanation, complete explanation for everything. Some of it is fault on our end, when we ask for things we shouldn't ask for, and as I mentioned, that is about 8 percent of those letters we send out, so about 5 to 6 percent

of the 510(k)s we are asking for things we shouldn't ask for, so we are putting in procedures to actually make sure that doesn't happen because it should never happen, but we do have companies who are submitting applications that are deficient. I am talking about big concerns where we put out guidance document, it has been out for years, and says exactly what to do, and the company doesn't do it and doesn't provide a justification not to do it.

At the same time, we also need to have better clarity on expectations. I would like to have more guidance out there. We know when there is guidance, you are more likely to get your device cleared and cleared quickly, but we need the capability to do that. I need a core team of writers and I need sufficient number of experts to do the reviews and do the guidances and get them out quickly. That can make a big difference.

Mr. GREEN. And you don't have that ability right now?

Mr. SHUREN. We do not have sufficient ability.

Mr. GREEN. Is it just based on funding? I know others members have asked questions about that.

Mr. SHUREN. It is funding. To the extent we can make our own systems more efficient, we are doing that. We are doing what we can with what we have. We can do more if we have more, and we can do it right.

Mr. GREEN. What some of us are hearing, particularly medical device companies are saying there is a lack of consistency and predictability in the process and sometimes the rules change in midgame, and believe me, the FDA would not be the only federal agency that does that. I can talk about a lot of agencies. Certainly it is hard to put a quality submission together, but is that also a problem that sometimes once a submission is made, like you said, you may be requesting information that you don't really need or do the rules actually change once somebody submits?

Mr. SHUREN. Sometimes the rules change and it is justified, there is a new safety concern and we go back to the company and say we have new information and based upon that we need additional information, or based on the company's own data, we have found a problem and we send them back. What we are now instituting is, when the rules of the road change and they need to change quickly where we can't take time to get public comment because of major public health concerns, we are now going to put out a notice to industry to say things are changing, here is why and get it out quickly, where before companies wouldn't find out until they came in the door with their submission and they wasted their time and effort when they could have been notified earlier, and we are fixing that.

Mr. GREEN. I guess just the certainty and consistency, that is what anybody wants.

I have heard you say previously that the FDA is meeting its user fee goals for 95 percent of the submissions. When I looked at the charts from the most recent quarterly update on the medical device performance goals, there was an awful lot more goals in the 5 percent that were not being met, and I know that the 510(k) submissions account for about 95 percent of the device reviews that FDA does each year but all these red boxes where the FDA is not meeting its user fee goals are concerning to me. I also note that goals

aren't being made, largely the PMA goals. In the previous panel, we heard from patients who could not access these breakthrough technologies and had to leave the country to get access. What are you doing right now to rectify that situation and what steps is FDA taking to ensure that patients have access to this cutting-edge medical technology?

Mr. SHUREN. So in addition to the actions I already mentioned about making these systems more predictable, more consistent and more efficient, the other things we are doing are, we need to adjust clinical trials in the United States. If we can start clinical trials earlier here, we get the technology earlier here, companies then keep the technology with our doctors, so we are going to putting out a policy soon to actually allow for the first time you give it to a patient, to let those studies start earlier than we did in the past and to allow for the manufacturer to make changes, to innovate and test without necessarily coming back to the FDA. We heard this is a big deal for the VCs, it is a big deal for the companies. We will putting out that policy.

The other is being very clear about the factors we take into account when we make benefit risk determinations. We had been inconsistent in some cases when we do that. We are for the very first time going to put out what those factors are. We are going to get public comment on it, things like taking into account a patient's tolerance for risk. Serious disease patients are going to be willing to tolerate more risk. Serious disease, we may allow for a treatment, particularly if there is not an alternative out there. That guidance will go out. We will require that our viewers go through those factors. They lay out what the answers are and they put in the record. I consider that so important that actually I chair that working group personally.

Mr. GREEN. One quick question. I would like to know, we have heard a lot of comparisons to the European system and ours. If there is a device in Europe that has been approved even with those 74 or whatever they do, can the FDA assess the success or failure of that device in Europe and do you give any substance to the quality of any studies that come out of those that are actually being used in Europe?

Mr. SHUREN. So we absolutely will use data from Europe or from other countries. We do use that data all the time. In some cases, we have even approved devices that are based predominantly or, to my understanding, completely on data outside the United States, but it has to be the data that actually answers the question, and one of the challenges with Europe and other countries is, they will let a device on the market without showing it is effective. So they actually never generated the data to show it is effective to meet the U.S. standards, and a lot of those studies are not so robust. In fact, the British medical journal in a series of investigative articles, the European Society of Cardiology, a group of European health technology assessment agencies all came out and said for high-risk devices, you should be more like the United States. You should show you are effective. You need to have more robust clinical studies like the United States. You need to be transparent like the United States. Tell doctors and patients the basis of those decisions and put out more guidance explaining what you need to do. As much

as we need to do more guidance, the EU puts out nothing near what we do to clarify what kind of studies you have to perform.

Mr. GREEN. Thank you for your patience.

Mr. TERRY. Mr. Scalise, or is it Dr. Scalise?

Mr. SCALISE. I am not a——

Mr. TERRY. You are recognized for 5 minutes.

Mr. SCALISE [continuing]. Juris doctor or a medical doctor. I just play a Congressman on C–SPAN occasionally here.

I do want to ask a few questions going back to your testimony, and in a few different sports you talk about the success of the FDA, and specifically in relation to what is happening in Europe, and of course, we had a full panel this morning that was giving I think some very eye-opening, riveting and not real positive glowing endorsements of FDA's performance, especially compared to Europe, and you say here "In terms of time to market, data shows that the United States is performing as well or better than the European Union," and then you go on to say, "The EU typically approves higher risk devices faster than the United States because unlike in the United States, the EU does not require the manufacturer to demonstrate that the device actually benefits patients." You had a whole panel of patients sitting here at this table talking about devices they have access to in Europe that they would have to go to Europe to get that would actually improve their lives. Some actually did it. They went to Europe to get the device. You had Dr. Fischell sitting right there with a device sitting in front of him that has been waiting on FDA approval for years that relieves migraine headaches and yet there is data, there is devices, there is real testing, there are patients that use it and there are people that are using it in Europe, and you are implying that Europe has just got some of Wild West mentality that they are just giving out approval for things when in fact you have got Americans that right now have to go to Europe to get the treatment that actually would and has in some cases improved the lives of those patients. So how can you make those comments, especially after you sat here and heard the statements from these patients and the mother of a patient?

Mr. SHUREN. So I can have chart 3, first of all, I empathize with the patients. I am a physician and a patient myself. I have loved ones who are patients. I want to get safe and effective devices but emphasis on safe and effective devices to patients, patients even like myself.

You asked in terms of the data for performance. This isn't my study, this is an industry study. They looked at the 510(k)s without clinical data. That is about 80 percent of the devices that we review, and the products came on the market first in the United States as often or more often in the United States than they did in the EU, and in fact, if you looked at the top chart, the performance, the likelihood of coming on the U.S. market first actually has improved more recently in time.

Now, for the smaller group of high-risk devices, they have come on the market first in other countries for years. We can do better on that. We can get a lot closer. But we will never be completely as fast because of that difference in effectiveness. Does it have ramifications? Yes, because you do put on the market devices that don't benefit patients, patients get in some cases when they have

alternative that works so they missed out on good therapy. The health care system paid for ineffective treatments. And in fact——

Mr. SCALISE. I want to go back to something, though, because again, we had testimony not just from patients but from doctors who have actually invented devices. I mean, Dr. Fischell, this is somebody who has been inventing devices for decades, has been nationally recognized, inventor of the year, has put out more devices than most doctors in this country, and he first talked about the change he has seen in the attitude in the FDA is the last 2 years is the worst he has seen in his 42 years of inventing, and then he further went on to say there is a different attitude at the FDA than we have ever seen before. This isn't—you know, you can show metrics all day long but instead you have patients who are sitting here and you have got inventors who are sitting here saying the problem they are seeing in the last 2 years isn't something that they have seen before at the FDA, and they surely aren't agreeing with your glowing metrics that you can go find somebody to say how great you are doing when you have got real inventors, real patients sitting here saying the job is not getting done. You know, they will tell you if you want to look at data and compare it to Europe and say what Europe has or doesn't have. They will say that firms are willing to submit whatever data you want but they can't get the certainty in the regulatory process from your agency. They want to know how to comply. They can't even get the certainty from you to know how to comply.

And so you can sit here and talk about all the data you are not getting and all the money you are not getting and all the turnover you have got. I can tell you, I mean, I have looked at your budget. Congressional Research Service actually issued a finding that the medical device review process funding in your agency has increased 35 percent in the last 2 years. You show me a family out there as families are cutting back you have got a 35 percent and you have the nerve to sit here and say you are not getting enough money and the reason you can't move things fast enough is because you all have too much turnover. Let me tell you, I have looked at agencies and especially if you talk to people in the private sector, they will tell you, if you have got turnover problems, that is a management problem. You can't blame that on somebody else. You can't say you are not getting enough money. You got a 35 percent increase over the last 2 years, and oh, by the way, during that time, the average review time increased by 43 percent. So maybe cutting back to what you were at when you were actually getting some things done might be the most prudent approach as some of the patients here said, and so to say that you don't get enough money, you got a 35 percent increase. The delays are increased. You have got some management problems I think you have to recognize before you blame the patients and the inventors who are sitting here and some have to go to Europe to get the relief that they have gotten. They actually went to Europe and got the relief and you still haven't approved the devices here.

So real changes have to occur and you can't just show metrics that say how great you are doing or say you need more money. I mean, you know the environment here. We are broke. We are trying to figure out how to do more with less because we don't have

the money. We can't borrow it from China anymore and, you know, there has got to be real changes. But you can't blame other people either.

Mr. TERRY. Thank you.

Mr. SCALISE. I will yield back the balance of my time, whatever that balance is, Mr. Chairman.

Mr. TERRY. Dr. Christensen, you are recognized for 5 minutes.

Mr. CHRISTENSEN. Thank you, Mr. Chairman, and Dr. Shuren, thanks for your patience today.

Let me at least try to help you answer the question about what is happening with venture capital because the ranking member earlier reported that Bloomberg News today reported that in the first quarter of this year, venture capital for medical device and equipment makers went up 20 percent. That was $841 million in 90 deals, so the first quarter it went up.

But let me try to ask you a question about some other things that have been discussed today. In this hearing and in previous hearings before the committee, we have heard from a variety of industry sources and supporters of weaker or less rigid regulation about a flawed FDA regulatory process for medical devices. We have heard a lot about two industry-funded studies in particular, one by Dr. Josh Makower and one by the California Healthcare Institute. These studies were critical of your agency, purporting to show that the FDA process causes undue delay in approvals. We asked leading medical experts to provide us with their views on the methodology of these studies, and we asked FDA to provide the views of the agency. So Dr. Shuren, first, can you tell us about the FDA's views on the findings of the Makower and the California Healthcare Institute studies?

Mr. SHUREN. So we did have concerns about the methodologies that were used. For example, in the Makower study, he sent out a survey to 1,000 companies, not to the full industry. Of that, he got 204 who responded, and then on particular questions trying to compare the United States to the EU, at most, the number of people who could actually had a device in both might have been 60 to 80. So very underreporting, and in those cases, we know the people who are most dissatisfied, that is who reports. Most of these companies did not have much experience with the FDA. Only 55 percent brought a 510(k) through the process, only 32 percent a PMA.

Much of the methodology to compare time frames was apples to oranges. They didn't look at the same point in time between the EU and the United States. They compared a first communication with the United States which could occur before you even do a clinical study where in the EU your first communication may be before you actually submit the application. And therefore I could reduce those times dramatically if I didn't meet with companies and just say give me the submission and our times would dramatically improve. In fact, the best way to compare is, if we had the data from the EU and comparable times for reviews, and in fact it doesn't exist because the EU doesn't keep it and doesn't report it.

Mr. CHRISTENSEN. Thanks. Well, your views are really similar to the views of the outside experts that are described in the supplemental memo that was shared today. These experts also identified a variety of problems. One reviewer concluded that there so many

flaws in the design and execution that the author's conclusions are rendered essentially meaningless. Another reviewer concluded that the CHI study reflects little or no understanding of the complexity of medical devices. All reviewers indicated that these studies would not stand up to basic scientific peer review.

So Dr. Shuren, would you agree that these industry studies are so flawed that they should not be used as the basis to justify a radical change to the FDA device safety standards?

Mr. SHUREN. I would not be using them in terms of the actual numbers and data behind them, and that is why we tried to actually go and pull what the real numbers look like. On the flip side, in some of the studies that have come out, they raised what concerns are and some of the problems that are raised like high turnover rate, insufficient guidance, those are issues that we agree need to be addressed. That is why we are taking the steps that we are taking, but we shouldn't base decisions based on flawed data. That doesn't serve anyone well.

Mr. CHRISTENSEN. I agree.

Mr. Chairman, we have important decisions to make on this committee as we work towards reauthorizing the Medical Device User Fee Act, and we can't really afford to base these decisions on fatally flawed and biased studies.

Mr. SHUREN. If I may just say quickly, by the way, that chart is from one of the flawed studies, and I put it up because, you know, if you put it out there, it is out there. It is not my data, that even industry in their own study reported what comparisons between the United States and the EU, so just that is on the record.

Mr. CHRISTENSEN. I am just curious. I understand that Europe might be forming some kind of unified committee to more standardize their review of their medical devices and probably medication. Do you know anything about that and how close they are, and might that not make a difference in how FDA might accept some of the data?

Mr. SHUREN. Ultimately, I don't know what the EU will decide. We should find out in 2012. But they have been going through a whole process to review their own system because of complaints that were about it, about not uniform, inconsistent, not providing adequate patient protections. In fact, the clinical director for the UK counterpart to my agency just last year said I am appalled at how many devices are brought to market with a lack of appropriate clinical data. The fact that much more clinical data and evaluation is needed and the notified bodies, there are over 70 private companies, do not know how to adequately assess or challenge clinical data or tell those companies relying on equivalents that they actually need to do a clinical investigation. These are commercial organizations, many of whom are reluctant to challenge because they fear losing their clients and for their survival, and these are one of the things leading to that review in the EU and maybe potentially changes over there, and that is the call you heard from the European Society of Cardiology and the British medical journal to actually in some respects make some things more like the United States.

Mr. CHRISTENSEN. Thank you. Thank you, Mr. Chairman.

Mr. STEARNS. The gentleman from Virginia, Mr. Griffith, is recognized for 5 minutes.

Mr. GRIFFITH. Thank you, Mr. Chairman.

I was pleased to hear you talk about tolerance for risk, and if you have a high-risk patient, they are more willing to take—you know, the patient who has got a serious illness willing to take some risk. I am wondering if the reverse is true in relationship to the treatment, and it sounds like it isn't, because I heard you talk about the European and some of the doctors said on a high-risk device they wish it was more like the American systems. But I am thinking about low-risk devices. I am thinking about Ms. Sagan's testimony when I say this, because, you know, as long as there is a caveat or a statement that says, you know, this hasn't been through 50 years of marketing or testing on humans, her daughter would be in a much better shape to have something that would shut off the insulin pump and the daughter would know and her mom would know that, you know, even if it doesn't work, it is better than what they have got right now. Even if it doesn't work 100 percent, it is better than what they have right now.

Every human being is different, and I would point that out to you because we had testimony from the other lady that she had the migraine fix for her 5 years ago, if I remember correctly—I may be off on the number of years—but years ago because she was part of a trial, and for 9 months she had a normal life, and it sounds like in listening to that testimony this morning that that was a fairly low-risk medical device that could have been brought to bear, and everything isn't going to work for everybody, and having a huge study that says it is effective for 99 percent of the population isn't always going to be the way to go.

I did a little data research, you know, on accidents in ambulances, and I am not going to ambush you with it but I will just tell you about it. Because if you take the theory that I was hearing this morning that we have a certain number of deaths, we had 300 deaths in an 11-year period in automobile accidents while people were in ambulances. We had 24 deaths in a single year with med-evac. Well, if you took that and applied it to what the FDA has been doing from what I heard in testimony today, that means you wouldn't allow the med-evacs or the ambulances to be out there because notwithstanding the fact that it might help thousands of people, some people died. And I understand that you have to be careful but you have to take that into account. And so I would have to say to you that you might want to look at a risk-versus-benefit analysis and if the risk is low and the benefit might be great, get that thing out there quicker because, you know, we heard testimony from people who are suffering who could really use some help, and I understand, if you are putting something inside somebody's body that is going to be there for hopefully 20 years, that is a different situation. I understand what the Europeans are saying about high-risk devices. But we were hearing testimony this morning about devices that sounded like to me—now, I am a lawyer, not a doctor, and maybe I wrong, but it sure didn't sound like they were high-risk devices to me, that it seemed more high risk not to have, for Ms. Sagan's daughter not to have something that at least—you know, even if it worked most of the time would shut that insulin off. That

doesn't mean she still wouldn't have risk because she is diabetic but it would seem to me that that would be the better course, and I don't know how you fix that, and if you need us to help, come see me, I will do what I can.

That being said, I would also say in regard to venture capital that Chris Coburn, the head of the Cleveland Clinic Innovation, stated last week raising capital is harder, given the current economy and health care reform creates a lot of unknowns. Raising capital is harder. Health care reform creates a lot of unknowns in the current timeline. You add in regulatory delays and all of a sudden the arithmetic of developing products domestically starts to break down. So it is not just folks coming in here with some kind of a political agenda, this was just a talk that he was giving somewhere, and I am just wondering if you would submit them later because my time is almost up what steps you might be taking on all of these things that I have mentioned.

And then also I would say apparently at a recent hearing of the Committee on Oversight and Government Reform, you mentioned that sometimes reviewers ask for data that might not be necessary, and I am wondering what you are doing about that because the industry indicates that is a relatively recent phenomenon. We heard testimony this morning that one of the parts on the migraine invention that Dr. Fischell was talking about, he said he had a plastic valve he showed us, and he said this is already used in all kinds of different devices but now I have to show them it works again, even though it has already been approved in other devices, just that valve, and I am just wondering what steps you are taking to correct that. Where would people have gotten the idea that asking questions like that is acceptable, and do you have a process in your industry if you have different teams looking at different things to say well, wait a minute, team A already approved this valve and it looks like it is pretty good.

So I would ask you to submit those to us for the record and so that I can review those as well, and I know I fired a lot at you and I only have 19 seconds for you to respond, but anything you want, you can say.

Mr. SHUREN. Well, I will give you an example of some of the things we are doing to ensure we make the right decision and consistent. So if you are going to the review team says we want to ask for a new kind of study for a type of device, that is being brought to this new center science council so rather than a decision made low down in the organization, it is coming up to the senior managers and experienced scientists and medical officers to review to make a call as to whether or not that is right. That allows for looking over the program for consistency, to make sure that decision is well informed because we may turn around and say we disagree. Those are the kinds of changes we are putting in place that if you are going to make a change, it has to be made at the right level in the organization. I still want to give my reviewers flexibility, but when big decisions are being made, I need the right people to be involved in making that call.

Mr. GRIFFITH. Thank you, Mr. Chairman.

Mr. STEARNS. All right. The gentleman's time is expired. I think we are going to do a second round and then you are free to go, so we appreciate your waiting here.

Just to be clear, you are citing what appears to us as a flawed study in your testimony, what you said in your opinion in your testimony and on the report here. Is that right? Does that make sense to you?

Mr. SHUREN. Oh, yes, for the California Healthcare Institute?

Mr. STEARNS. Right.

Mr. SHUREN. Yes, I do think there are parts in terms of some of the data they provided that I would disagree with and how it is presented.

Mr. STEARNS. OK. I just wanted to put that on the record.

The gentleman from Texas, Dr. Burgess.

Mr. BURGESS. Thank you, Mr. Chairman.

Dr. Shuren, thank you for staying with us so long. Part of the review of the 510(k) process, the FDA allocated $1.3 million to the Institute of Medicine to convene a committee to evaluate the 510(k) effect on patient safety and innovation. The IOM committee will have a very influential role including reviewing seven of the FDA's most controversial recommendations. Now, in February of this year at a Health Subcommittee hearing, you seemed to have some concern that the IOM committee itself would lack the patient advocates, innovators and inventors who are familiar with the 510(k) system. Critical omissions raise questions as to credibility of the IOM recommendations and why the FDA would pay $1.3 million in taxpayer money for such recommendations. Is that a fair observation?

Mr. SHUREN. I don't think I had raised concerns about it. I think some of the members were raising concerns in terms of the panel makeup. And what I did try to put out at the time is——

Mr. BURGESS. Are not our concerns your concerns?

Mr. SHUREN. Concerns by the members, some of the members who are on the committee.

Mr. BURGESS. They should be your concerns. If they are our concerns——

Mr. SHUREN. Well, I understand, and what I tried to say too is, we contract with the IOM. We don't make a decision in terms of who are on the panels or what they look at. I will tell you, though, that, what comes back from them are recommendations. They are not making a decision; they are recommendations. And if they make a recommendation, if we are thinking of adopting it and it would have an impact, a big impact on industry or others, we will go out and seek public comment first. If it is a recommendation that pertains to legislation, that is not our call.

Mr. BURGESS. Have they made recommendations to the FDA?

Mr. SHUREN. No, I have not seen anything from the IOM yet.

Mr. BURGESS. Now, there is a lawyer from the University of Minnesota named Ralph Hall who has concerns that the IOM committee violates the Federal Advisory Committee Act. Are you aware of that opinion from Dr. Hall?

Mr. SHUREN. Yes.

Mr. BURGESS. And if that is the case, it would be illegal for you to implement the recommendations of the IOM committee that violated the Federal Advisory Committee Act, correct?

Mr. SHUREN. I think he raised the concern of, is the committee fairly balanced, and there are people on that committee who have experienced developing 510(k)s to come to the agency, there are people with experience dealing with 510(k)s within the agency.

Mr. BURGESS. Did the IOM committee certify that it had complied with section 15 of the Federal Advisory Committee Act?

Mr. SHUREN. I don't know if they certified.

Mr. BURGESS. Well, but you are telling us today that you will not institute any of the IOM committee recommendations until some of these questions are resolved?

Mr. SHUREN. I will not implement any of the recommendations if we wanted to adopt, there would be recommendations we may decide we are not going to adopt. But if there are recommendations that would have a big impact on industry or others, we would seek public comment before we would proceed.

Mr. BURGESS. But why spend $1.3 million to a committee that doesn't have patients and doesn't have anyone with any medical device-related experience, especially innovators?

Mr. SHUREN. The Institute of Medicine is a well-respected, well-regarded organization that government has turned to, Congress has turned to many times for outside——

Mr. BURGESS. But shouldn't they have at least one patient representative on those committees?

Mr. SHUREN. I would direct to the Institute of Medicine in terms of the decisions made.

Mr. BURGESS. And again, I would direct your attention to the overall legality of whether or not they complied with section 15 of the Federal Advisory Committee Act.

Let me ask you this. There are complaints that the FDA has not communicated with companies what is needed in the submissions. The FDA is not telling companies in advance, and what will happen is, 50 to 75 days later after the submission you all will come back with what was needed in the submission, so obviously that upsets and frustrates the companies because of the added time, and I think we heard Mr. Bilbray comment on that fact. What are you doing to ensure that companies are notified in advance about what is needed and then thereby included in the submitted applications?

Mr. SHUREN. First, I would say there are other occasions where companies know what to do, we have told them what to do, and they don't do it, and I appreciate the fact of hearing that companies will provide us what we need to receive, and I have heard that before, but we have companies that actually don't do that. They don't give us, even in spite of laying out what they need to do. I will give you a very quick example, something called the pulse oximeter that actually——

Mr. BURGESS. I know what it is.

Mr. SHUREN. And you know what it is, just for the other members. It is a sensor you can put on your finger and it will tell you how much oxygen is in the blood. We have had guidance since, I believe, 1992. We updated it in 2007. It said you need to do a very

simple clinical study. It is sort of you use this and you measure from the blood and see if it is accurate. We recently had a company come in, didn't send us any clinical data, and we go back to them, why not, and we ask again, where is the clinical data, we have laid this out for years. We do deal with those circumstances, so it goes back and forth.

For the cases where we can provide more clarity, I would like to be able to put out more guidance for industry and to update our guidances more quickly. I would like to have the capacity to go ahead and do that.

Mr. BURGESS. And I think we would like for you to do that. I would like the assurance that a company comes to you with a novel device and says what are we going to need to do to comply with your guidelines to get the submission completed in a timely fashion. I would like to be certain that they are getting that information upfront the first time and it doesn't change throughout the submission of that application.

Mr. SHUREN. Well, one of the things we are doing are what we call pre-submission meetings if you come in, let us say, before you are going to do a clinical trial or before you submit your application. We are going to be putting out guidance probably by November that now for the first time it lays out here are the expectations for company, what they have to give to us, here are the expectations of what you can expect to see from the agency, and that includes our putting down what is our advice, and then standing behind it, assuming that device doesn't change in an important—you change what the use is for, you change the technological characteristics that may have been. But if not, then we should be standing behind it and that is going to be put out in our guidance later this year.

Mr. BURGESS. And on your Web site?

Mr. SHUREN. The guidance will be on our Web site. In fact, it will be out for public comment before we finalize it. All the things I am talking about from guidance, all go for public comment. In fact, some of the things we don't normally put out for public comment we are doing like that notice to industry letters, which is an internal action, we put out standard operating procedures of what we would do and when, we asked for public comment on it. It is out right now for folks to weigh in.

Mr. STEARNS. The gentleman's time is expired.

The gentlelady from Colorado is recognized for 5 minutes.

Ms. DEGETTE. Thank you very much, Mr. Chairman.

I just want to ask you a couple of follow-up questions, Dr. Shuren. The first one is, the question about the funding levels because the chairman had said in April 2010 there was a CRS report that said the medical device review process funding increased from $275 million in fiscal year 2008 to $368 million in fiscal year 2010, but that funding as I understand it includes user fees. Is that correct?

Mr. SHUREN. Yes, and I believe that is more than for my center because my numbers for my center are a little bit lower.

Ms. DEGETTE. What are your numbers?

Mr. SHUREN. What I have from my enacted and my total budget for 2008 is $225 million, and this is what I am given from my

budget people, and from 2010, it is $272.7 million, and that is comprised of appropriations and user fees.

Ms. DEGETTE. How much of that is user fees? Do you know?

Mr. SHUREN. So in 2008, the enacted amount is $26.6 million, and the amount in 2010 is $32.8 million. And I say enacted because under the law, if we collect more than we are supposed to in the first 4 years, we have to give it back by lowering our fees in 2012, and in fact we are going to be doing that. Fees will go down in 2012.

Ms. DEGETTE. Now, when we enacted the user fees in the MDUFA legislation in 2002, that allowed the funding to increase in better proportion to the costs of the agency. Is that right?

Mr. SHUREN. That is correct. There was an adjustment factor after our workload went up we could increase accordingly. That was taken out in I think 2005, 2006. It remains in for the drug program. They can adjust accordingly.

Ms. DEGETTE. Would that be something that would be worth having the larger committee look at when we go towards the reauthorization next year?

Mr. SHUREN. We should look at how to account for increasing workload. I would like to provide user fees predictability for industry. I know that is important. But we also need to make sure that if our workload goes up, we get the sufficient resources to meet the workload. Otherwise we are not going to be able to meet our timeframes.

Ms. DEGETTE. So a lot of the device companies have expressed to me concern that if the user fees are too high and if we—and this is same thing actually the drug people say is—if they are too high, that that freezes out a lot of innovation and a lot of the kinds of creative devices that we might really want to see. What is your reaction to that?

Mr. SHUREN. Well, you have the ability to actually adjust the fees accordingly, dependent upon even for the type of company. I will tell for a 510(k), full fee right now is about $4,300. For a small business, and a small business is $100 million or less in annual sales receipts, it is about $2,100 for a 510(k).

Ms. DEGETTE. So that is not really an onerous fee.

Mr. SHUREN. PMA is higher. It is about $236,000 for full. For a small company, it is $59,000. A lot of the PMAs tend to come from the bigger companies. More of the 510(k)s come from the smaller companies.

Ms. DEGETTE. OK.

Mr. SHUREN. Which is why we developed the fees as we did. That is what we worked out with industry to spread that cost.

Ms. DEGETTE. Now, in the budget that some of my colleagues were talking about that was approved by the House and not the Senate earlier this year, the overall FDA was cut by about 10 percent under H.R. 1. Were you given any indication if that budget went through how much of those cuts would go to your agency?

Mr. SHUREN. For my center, my understanding is that if you take how much would be cut plus not getting the increases for a fixed cost like my rent goes up every year that I have to pay but it is out of my control, it is about 12–1/2 percent.

Ms. DEGETTE. You would be cut by 12–1/2 percent. Do you think this would have an effect even with some of these user fees on your ability to expedite some of these applications?

Mr. SHUREN. Yes, it would have an impact on our ability to do reviews. I mean, we can cut the funding. We cannot increase user fees but then people have to manage their expectations as to what kind of device program they are going to get. The drug industry said you know what, it is worth it to us. A robust FDA gets us better performance and we can see that today.

Ms. DEGETTE. And that was proven to be correct, right?

Mr. SHUREN. That was proven to be correct, and I understand the unique circumstances of the device industry. I honestly do. But then we have to figure out some way to have the right program, and if it is not there, then people need to understand, you know, what you get in return.

We need to do a better job at the FDA. We know that. We are doing it. That is what I am talking about today. There are some things we need industry to work on and then we need adequate resources to do it right. That is good for companies. It is ultimately good for patients, and that is what this is all about.

Ms. DEGETTE. I think that is kind of a good place to end it, Mr. Chairman.

Dr. Shuren, I appreciate your candor with this committee and your ability and willingness to discuss the deficiencies at the agency, and I think all of us really need to sit down with you as we move towards the reauthorization next year of the user fees to talk about what we really need to do to make it work because there are a lot of devices out there that can save lives and we want to make sure that they are reviewed quickly, that they are reviewed thoroughly, that they are safe and they are approved. So thank you very much.

Mr. SHUREN. I appreciate that, and I would like to have the ability to work with you all, and I also hope that if the things we are talking about are right, to also have your support as we move forward.

Mr. STEARNS. Dr. Shuren, I would expect, you know, maybe we will have another hearing sometime in the future just to follow up with all these things you are saying. You know, obviously you mentioned all these things you are doing, and I think the turnover rate is something you have to figure out too because I think lots of times organizations where you work, turnover rate is low even though they are not paid a lot of money because of esprit de corps, because of the mission and the patriotism and whatever else, leadership is involved, so——

Mr. SHUREN. Well, we actually did an assessment in my center. The esprit de corps is actually off the charts compared to the rest of my government. My people are very committed.

Mr. STEARNS. I don't know if that is good or bad.

Mr. SHUREN. It is good in the right way. I will say, we have the same problem in the drug program. They had a high turnover rate. They were able to cut it and they have been able to maintain it low, and they did it with targeted retention allowances, by having enough staff to do the work, get away from a sweatshop mentality

and have enough managers and project managers to run that program.

Mr. STEARNS. Are all the guidances on FDA's Web site the current state of the thinking at FDA staff? If we go to that site, will we find the latest and the greatest state of thinking?

Mr. SHUREN. I would not be surprised if we have guidances that are probably not fully up to date.

Mr. STEARNS. So your Web site is not up to date?

Mr. SHUREN. No, the Web site is up to date as to the current guidance. I will say that we do run into cases where our thinking for that kind of device may chance and the guidance hasn't gotten updated in time.

Mr. STEARNS. All right.

Ms. DEGETTE. Mr. Chairman, just before we adjourn, some housekeeping. You had asked unanimous consent to put this Medtronic case into the record. Mr. Waxman had asked UC for this AdvaMed press release, and then we had asked UC for Dr. Shuren's slides. Are those all agreed to?

Mr. STEARNS. By unanimous consent, so ordered.

[The information follows:]

Quick Links: Skip to main page content Skip to Search Skip to Topics Menu Skip to Common Links

Premarket Approval (PMA)

510 (k) | Registration & Listing | Adverse Events | Recalls | PMA | Classification | Standards

CFR Title 21 | Radiation-Emitting Products | X-Ray Assembler | Medsun Reports | CLIA | TPLC

New Search Back to Search Results

Note: this medical device record is a supplement. The device description may have changed. Be sure to look at the original PMA to get an up-to-date view of this device.

Trade Name	MEDTRONIC SPRINT LEADS
Classification Name	Implantable Cardioverter Defibrillator (Non-Crt)
Generic Name	Transvenous,Steroid Eluting,Quadripolar,Active Fixation, Pace/Sense Ventricular Lead
Applicant	MEDTRONIC INC.
PMA Number	P920015
Supplement Number	S038
Date Received	09/12/2007
Decision Date	02/06/2008
Product Code	LWS [Registered Establishments With LWS]
Advisory Committee	Cardiovascular
Supplement Type	135 Review Track For 30-Day Notice
Supplement Reason	Process Change: Manufacturing
Expedited Review Granted?	No
Combination Product	No

Approval Order Statement
Approval for changing the molding vendor and molding process parameters for the is-1 connector sleeve component for sprint lead models 6930, 6931, 6945, 6947, 6948, 6949, and 6944.

For Immediate Release
July 20, 2011

AdvaMed Statement on the House Energy and Commerce Subcommittee Hearing on FDA Device Regulation

WASHINGTON, D.C. – Stephen J. Ubl, president and CEO of the Advanced Medical Technology Association (AdvaMed), released the following statement on today's U.S. House of Representatives Energy and Commerce Subcommittee hearing on the impact of FDA medical device regulation on American patients, innovation and jobs:

"The medical technology industry has long recognized that a strong and well-functioning FDA is vital to maintaining America's preeminence in medical technology innovation, and we support the current regulatory framework in the U.S. However, it is troubling that several recent studies have shown that patients in Europe often benefit from cutting-edge medical technologies months – and sometimes years – before American patients.

"While we are concerned with this trend and FDA performance in a number of critical areas, we believe that any steps necessary to address this situation can be taken without changing the current robust statutory standards for clearance and approval of medical devices.

"When FDA and industry work together so that patients have timely access to safe and effective medical technologies, it's a win-win situation for everyone. We look forward to working with the Administration, Congress and FDA to ensure FDA regulation of medical devices and diagnostics is both efficient and predictable, while maintaining the highest standards of safety and effectiveness."

###

AdvaMed member companies produce the medical devices, diagnostic products and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed members range from the largest to the smallest medical technology innovators and companies. For more information, visit www.advamed.org.

The Chairman cites an April 2010 CRS Report in his opening remarks that stated that the medical device review process funding increased from $275 million in FY2008 to $368 million in FY2010.[1] Theses statistics, however, are misleading.

- The funding that the Chairman cites includes user fees.
    - With user fees, the more submissions presented, the more funding increases.
- Prior to 2002, FDA's resources for its devices and radiological health program had increased at a lower rate than costs.[2]
- The enactment of user fees in MDUFA in 2002 allowed funding to increase in better proportion to costs.
    - This is the statistic the Chairman cites.

A more recent report of April 2011 states the $241 million (10%) cut under H.R. 1 for the FDA, as cited in Ranking Member DeGette's statement.[3] CRS has also noted that, "Congressional intent in authorizing user fees was that these fees would supplement—rather than replace—resources provided by Congress to FDA."[4]

---

[1] He cites either CRS Report, *Medical Device User Fees and User Fee Acts*, April 2010 or CRS Report, *The Medical Device Approval Process and Related Legislative Issues*, April 2010.

[2] FDA, "Medical Device User Fee and Modernization Act; Public Meeting," 72 *Federal Register* 19528, April 18, 2007.

[3] CRS Report, *Agriculture and Related Agencies: FY2011 Appropriations*, April 2011.

[4] CRS Report, *The Food and Drug Administration: Budget and Statutory History, FY1980-FY2007*, January 2008.

The Chairman cites an April 2010 CRS Report in his opening remarks that stated that the medical device review process funding increased from $275 million in FY2008 to $368 million in FY2010.[1] Theses statistics, however, are misleading.

- The funding that the Chairman cites includes user fees.
    - With user fees, the more submissions presented, the more funding increases.
- Prior to 2002, FDA's resources for its devices and radiological health program had increased at a lower rate than costs.[2]
- The enactment of user fees in MDUFA in 2002 allowed funding to increase in better proportion to costs.
    - This is the statistic the Chairman cites.

A more recent report of April 2011 states the $241 million (10%) cut under H.R. 1 for the FDA, as cited in Ranking Member DeGette's statement.[3] CRS has also noted that, "Congressional intent in authorizing user fees was that these fees would supplement—rather than replace—resources provided by Congress to FDA."[4]

---

[1] He cites either CRS Report, *Medical Device User Fees and User Fee Acts*, April 2010 or CRS Report, *The Medical Device Approval Process and Related Legislative Issues*, April 2010.

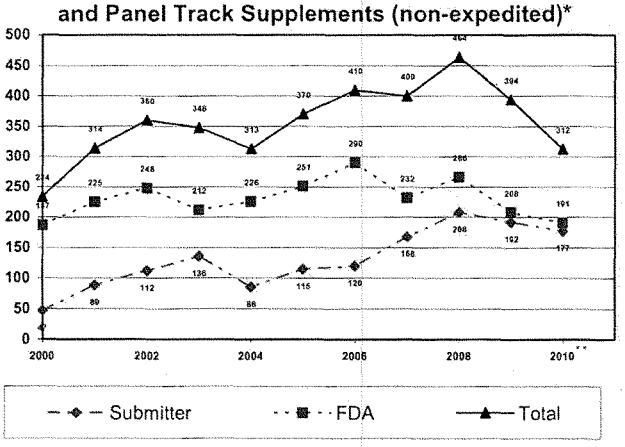
[2] FDA, "Medical Device User Fee and Modernization Act; Public Meeting," 72 *Federal Register* 19528, April 18, 2007.

[3] CRS Report, *Agriculture and Related Agencies: FY2011 Appropriations*, April 2011.

[4] CRS Report, *The Food and Drug Administration: Budget and Statutory History, FY1980-FY2007*, January 2008.

CHARTS:

1	Average Time to Decision – PMAs
2	Average Time to Decision – 510(k)s
3	CHI Report Fig. 14/15: Mean US 510(k) devices approval delay • Lag between EU approval and US clearance dates, by year • Percent Approved in US First / Approved in EU First, by increasing complexity
4	Percent of Submissions With AI Request (by year)
5	Percent of 510(k) Submissions with an NSE Decision Per Year
6	Workload Increased 27% since the end of MDUFMA I
7	Number of Submissions (IDE, 510(k), PMA), by fiscal year
8	Problems / Root Causes
9	Performance Impact Associated with Changes to MDUFA: % Completed Within Performance Target



*Times may not add to total due to rounding
** 2009, 2010 some cohorts still open as of July 5, 2011, data may change

CHART 1

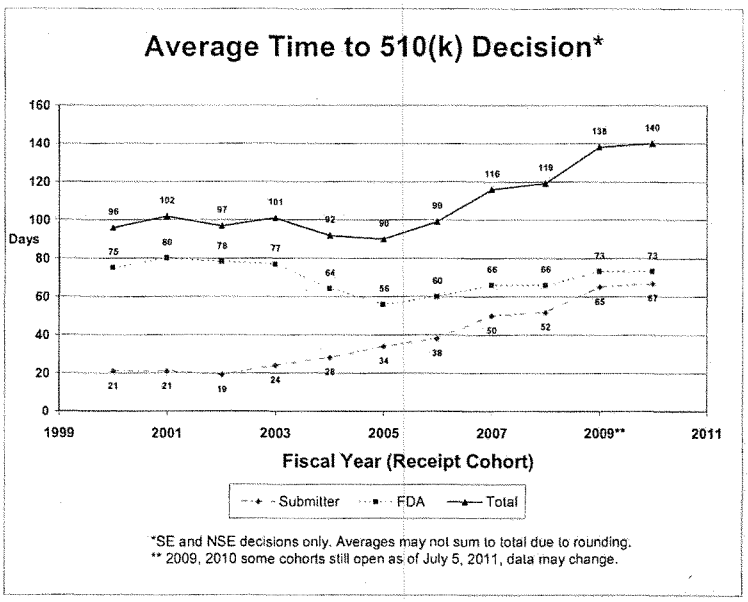
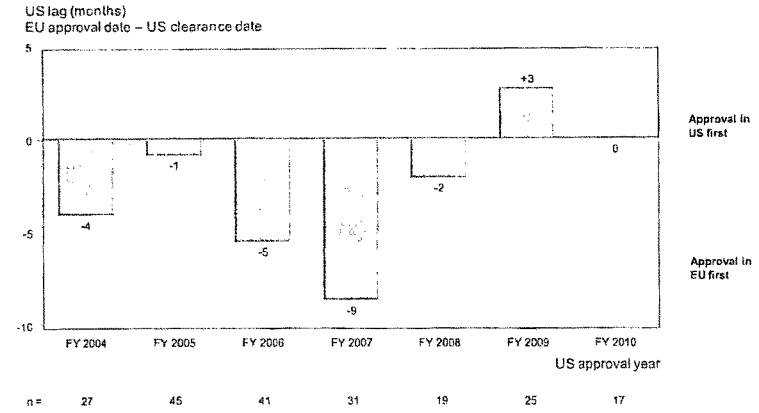

Average Time to 510(k) Decision*
Days
160
140
120
100
80
60
40
20
0
1999
2001
2003
2005
2007
2009**
2011
Fiscal Year (Receipt Cohort)
Submitter
FDA
Total
*SE and NSE decisions only. Averages may not sum to total due to rounding.
** 2009, 2010 some cohorts still open as of July 5, 2011, data may change.

CHART 2

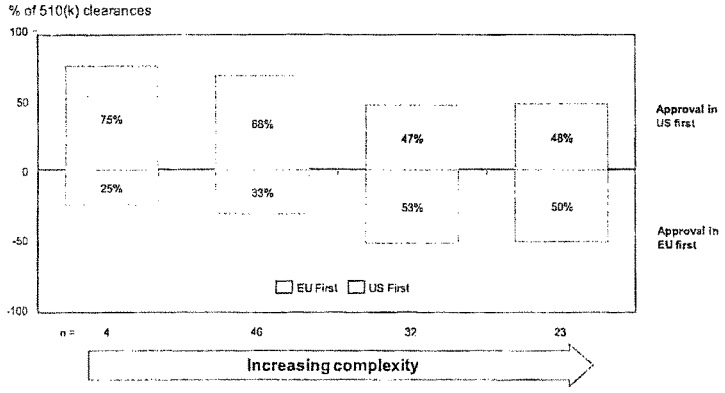
Mean US 510(k) devices approval delay (by US decision year)



Note: Represents original 510(k) application without clinical trials. Difference between 2004-2006 and 2007-2009 found to be statistically significant at the 5% significance level for probability of approval in US first, but not significantly for the mean lags. See methodology for more information
Source: Data compiled from 12 different medical device companies, where total sample size n = 205; BCG analysis

FIGURE 14. U.S. Approval Times for 510(k) Devices.

Mean US devices approval delay: 510(k) clearances 2004-2010



Note: Represents original 510(k) applications without clinical data. Devices classified using EU standard I-IIa-IIB-III where classification I is least risky while Class III is most risky
Source: Data collected from 10 different medical device companies, where total sample size n = 205 data based on 105 devices for which EU classification was available

FIGURE 15. More Complex Devices May Be More Likely to Be Approved in EU First.

CHART 3

SOURCE: California Healthcare Institute and The Boston Consulting Group Regulation: The FDA and the Future of America's Biomedical Industry" (Feb

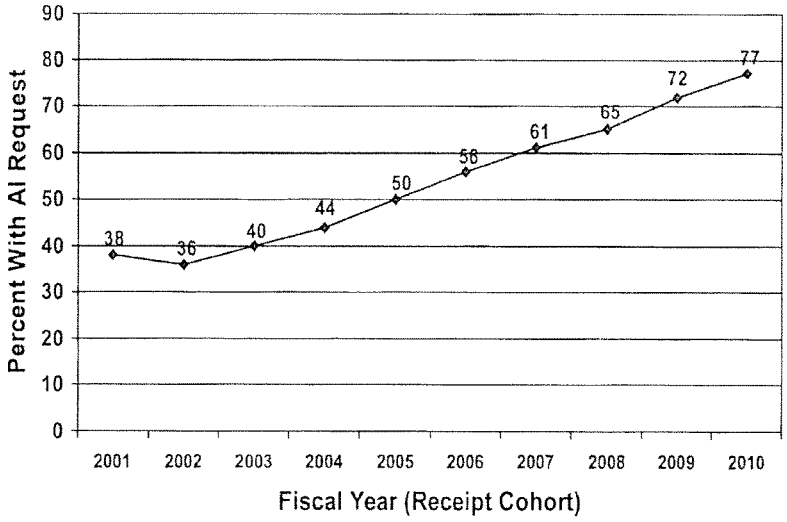

Percent With AI Request
90
80
70
60
50
40
30
20
10
0
38
36
40
44
50
56
61
65
72
77
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
Fiscal Year (Receipt Cohort)

CHART 4

Percent of 510(k) Submissions with an NSE Decision per Year

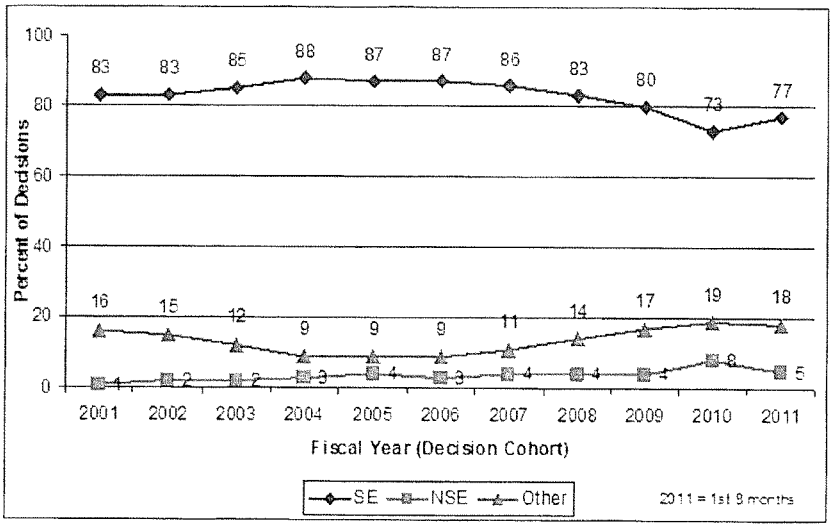
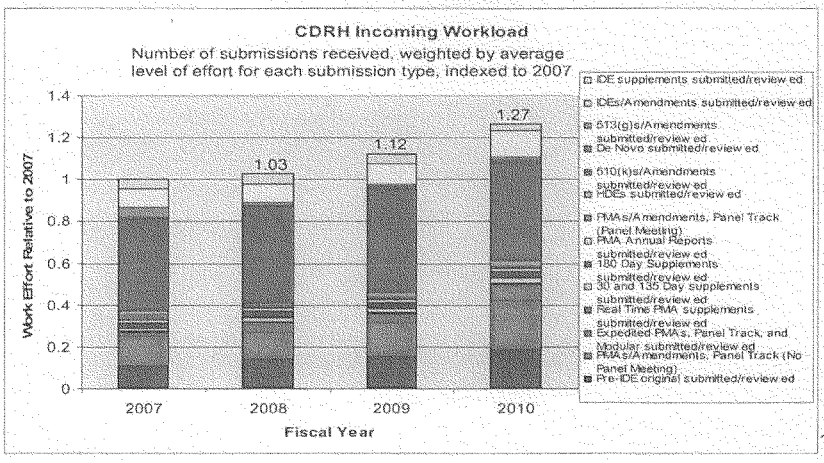


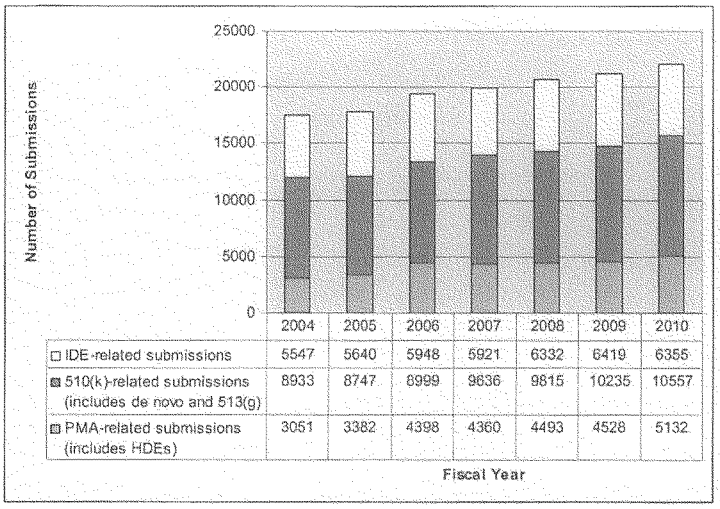
CHART 5

Workload Increased 27% since the end of MDUFMA I



12

CHART 6



	2004	2005	2006	2007	2008	2009	2010
IDE-related submissions	5547	5640	5948	5921	6332	6419	6355
510(k)-related submissions (includes de novo and 513(g)	8933	8747	8999	9636	9815	10235	10557
PMA-related submissions (includes HDEs)	3051	3382	4398	4360	4493	4528	5132

CHART 7

Problems:

The #1 problem is insufficient predictability

Clinical studies increasingly being conducted first abroad

Total time from submission to decision increasing for PMAs and 510(k)s since 2004 and 2005, respectively, and 510(k) deficiency letters and cycles increasing since 2002

Root Causes:

Changing, unnecessary, inappropriate, or inconsistent data requirements

Insufficient guidance and opportunities for FDA-industry interactions

High reviewer and manager turnover

Insufficient training

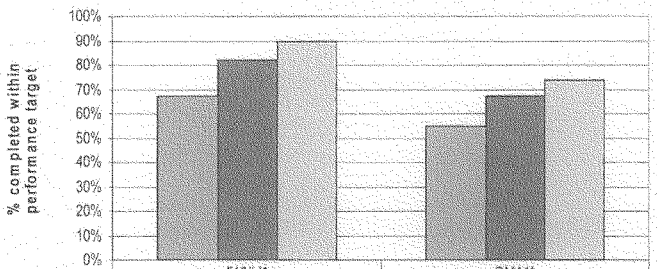
Inadequate oversight by managers

Growing FDA workload and increasing complexity of devices

Poor quality submissions

CHART 8

Performance Impact Associated with Changes to MDUFA:
Percent Completed Within Performance Target



	510(k)*	PMA**
No MDUFA	67%	55%
No MDUFA II	82%	67%
Current Performance	90%	74%

510 (k)s Performance Target: Complete reviews within 90 days
* PMAs Performance Target: Complete reviews within 180 days.

CHART 9

Ms. DEGETTE. Thank you.

Mr. SHUREN. May I just clarify one thing?

Mr. STEARNS. Yes.

Mr. SHUREN. But if the thinking has changed with the guidance, what we are trying to do is update the guidance first so people know but if not and we need to make a quick change because there is new information, there really is a risk you have to deal with, then we are going to these notice to industry letters, so that——

Mr. STEARNS. You have heard a lot of our panel today. I would think they would help you, and you are going to go to private industry first too. You are going to go there too, right?

Mr. SHUREN. For feedback on the process?

Mr. STEARNS. Yes.

Mr. SHUREN. We have already—it is out for anybody to comment on.

Mr. GRIFFITH. Mr. Chairman?

Mr. STEARNS. Congressman Griffith.

Mr. GRIFFITH. I was wondering if I could have just a minute to ask a question.

Mr. STEARNS. Sure, sure.

Mr. BURGESS. But before you do, because I have got—I just wanted to ask unanimous consent to put these two letters from Senator Kerry and the Massachusetts delegation into the record on the IOM study of the 510(k) process.

Mr. STEARNS. While you are looking from that, the gentleman from Virginia for 1 minute.

Mr. GRIFFITH. I heard you talk about your lease, so I am switching gears on you into something I am a little more comfortable with than medical devices, and I guess my question is, you said your rent goes up every year. I was wondering how long your lease was for and when was the last time you went and renegotiated with your landlord. Because I think it is something the federal government doesn't do. I am not picking on you all. I don't have any idea.

But a lot of times they just got locked into a lease and circumstances in the economy have changed, and when I took office I was able to cut the lease cost of actually more square footage, not as pretty but more square footage for about half the cost, and I am just wondering as your costs are going up, you might want to take a look at your lease and see if you can't renegotiate. Even if you are locked into a multi-year lease, you might be able to renegotiate.

Mr. STEARNS. That is good. That is experience talking.

We will put this in by unanimous consent.

[The information follows:]

Congress of the United States
Washington, DC 20515

March 1, 2011

David R. Challoner, M.D.
Institute of Medicine
Keck Center-W 825
500 Fifth St., NW
Washington, DC 20001

Dear Dr. Challoner:

We are writing in regard to the Institute of Medicine's on-going review of FDA's 510(k) clearance process for medical devices.

As you know, the 510(k) program has been responsible for clearing thousands of medical devices and establishing their safety and effectiveness for use by health care providers for over 30 years. The Center for Devices and Radiological Health (CDRH) has undertaken a review of the 510(k) program and in August of last year made 70 recommendations for changing the clearance process.

Last month, the CDRH announced action on some of these recommendations and has requested that the IOM review seven of the most controversial of the proposed revisions. This request is in addition to the overall review of the 510(k) process requested by the FDA in 2009. As work on both of these reviews continues at the IOM, we want to ensure that there is adequate opportunity for input from various stakeholder groups into this important process. These include: non-governmental regulatory affairs professionals from the medical device industry; medical device inventors and innovators, biomedical engineers and technical experts; and medtech entrepreneurs and investment and venture capital experts.

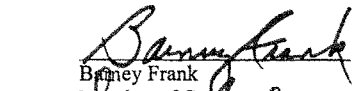
We urge you to allow substantive and meaningful participation by these stakeholders, as your review process continues this year. In addition, we ask that the IOM hold hearings for industry representatives to voice their concerns and provide written comments.

Finally, we would ask for a response from the Commission detailing what opportunities will be made available for all stakeholders to participate in the IOM review of the 510k) program. We feel the participation of these groups critical in order for the Committee to produce a fair, balanced, and credible assessment of the current 510(k) review process and make appropriate recommendations for improvements. Thank you for considering our position.

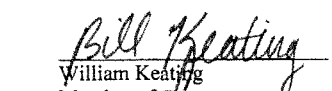
Sincerely,

Edward J. Markey
Member of Congress

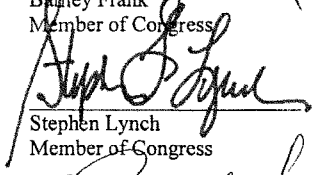
Michael E. Capuano
Member of Congress



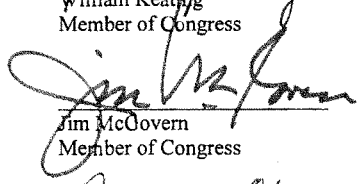
Barney Frank
Member of Congress



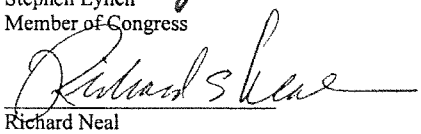
William Keating
Member of Congress



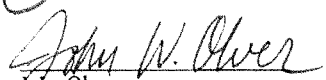
Stephen Lynch
Member of Congress



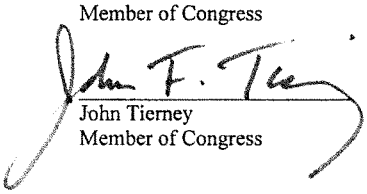
Jim McGovern
Member of Congress



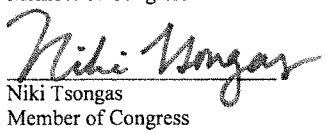
Richard Neal
Member of Congress



John Olver
Member of Congress



John Tierney
Member of Congress



Niki Tsongas
Member of Congress

JOHN KERRY
MASSACHUSETTS

COMMITTEES:
COMMERCE, SCIENCE, AND TRANSPORTATION
FINANCE
FOREIGN RELATIONS
SMALL BUSINESS

United States Senate

WASHINGTON, DC 20510-2102

April 13, 2011

The Honorable Margaret Ann Hamburg
Commissioner, Food and Drug Administration
U.S. Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Commissioner Hamburg:

I appreciate your efforts to reform the 510(k) medical device clearance process to provide more predictability, transparency, and stability to medical device manufacturers while maintaining the strong patient safeguards that citizens expect. I understand that the FDA is deferring the implementation of several recommendations until the Institute of Medicine (IOM) has completed their review. However, I am concerned that some of the recommendations that the FDA has forwarded to the Institute of Medicine (IOM) could be disruptive to the medical device industry and could have a chilling effect on growth, jobs, and patient access to medical innovation.

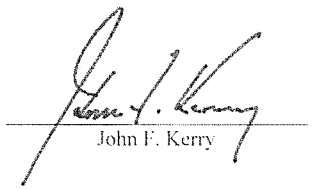
As you know, President Obama issued an Executive Order in January aimed at creating a 21st century regulatory system that protects the public while promoting economic growth, innovation, competitiveness, and job creation. The Executive Order said our regulatory system must promote predictability, reduce uncertainty, and rely on the most innovative and least burdensome tools for achieving regulatory ends.

Patient safety continues to be my highest priority, and I couldn't agree more that our regulatory framework must strike the right balance when it comes to increasing efficiency and transparency in the process. However, the medical device industry in my state has expressed concern that some of the recommendations would result in continued delays in 510(k) review times or would be unnecessarily burdensome and delay life-saving products from coming to market. Specifically, they have expressed concern that limiting the use of predicates, expanding the FDA's rescission authority, creating a new category of Class IIb devices, and changing key definitions and terms could place an additional burden on manufacturers and hinder innovation and economic growth.

I understand your agency's implementation plan defers action on these controversial recommendations until the release of the IOM's report. I have heard concerns that since the panel currently reviewing the 510(k) program at the IOM does not include representatives from the medical technology industry, they may not fully understand the impact of the proposed regulations on the industry. Given the concerns expressed, I urge you to establish a deliberative and transparent process for reviewing the IOM recommendations that ensures adequate opportunity to solicit substantive and meaningful input from all stakeholder groups before any recommendations are finalized.

I look forward to working with you on the important goal of reforming the 510(k) process in a manner that rigorously protects patient safety while maintaining our global leadership in medical technology. Thank you for your consideration of this request.

Sincerely,



John F. Kerry

Mr. STEARNS. Thank you very much for your patience. The subcommittee is adjourned.

[Whereupon, at 6:08 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Statement of Rep. Gene Green
O&I Subcommittee Hearing
Medical Device Regulation: Impact on American Patients, Innovation and Jobs.
July 20, 2011

Thank you Mr. Chairman for holding this important hearing today entitled: Medical Device Regulation: Impact on American Patients, Innovation and Jobs.

In 1976, the FDA was given the authority to regulate medical devices by Congress. Congress directed the FDA to categorize devices into three categories: Class 1, Class 2, and Class 3.

In order for a manufacturer to market and device for sale and use, they must demonstrate to the FDA the device is safe and effective for its intended use.

The manufacturers can do this through a pre-market application process or a pre-market application process, which is known as the 510 (k) clearance processes.

The 510 (k) clearance is used to bring devices to market that are substantially equivalent to a previous device that the FDA has already cleared for marketing.

The pre-market application process is more stringent than the 510 (k) process. The pre-market application can require clinical trials to demonstrate the safety of the device.

Much has been said by this committee over the past few sessions with regard to safety and monitoring of our food and drug systems at the FDA.

I would argue the device sector of the FDA has a good system in place to monitor the safety of medical devices.

But, I do understand the difficulties associated with the clearance process and the sometimes extremely long amount of time it takes to have a medical device approved by the FDA.

Today, our first panel will discuss the difficulties they faced when seeking treatment with a medical device in the US. These individuals often sought treatment outside of the US because medical devices are now being approved more quickly in other countries.

As a member who represents a part of Houston, home to one of the US's premiere medical center, the Houston Medical Center, this concerns me. I want to ensure the US is always on the cutting edge of medical technology.

Mr. Chairman, I look forward to hearing the testimony of our witnesses today and thank you for allowing us to discuss this very important issue.

Statement from Representative John D. Dingell
House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
"Regulatory Reform Series #5 - FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs"
July 20, 2011

Thank you Mr. Chairman for holding today's hearing.

Like most Americans I support creating jobs, promoting innovation amongst our medical suppliers, and ensuring safe and effective devices for those in need. But unlike my colleagues on the other side of the aisle, I do not believe that we can achieve these goals by gutting the funding we have tasked to do so.

I understand the industry having their concerns about FDA's medical device approval process. The approval process is critical to providing access to life-saving medical devices to patients who need them to live a full, healthy and balanced life. I have heard complaints about the increase in total review time, delays and inconsistencies in the review process, lack of clarity in data requirements, among other things.

Now I don't believe that throwing money at a problem will fix it, but I do believe that Congress and FDA cannot address these problems under the proposed budget offered by my Republican colleagues which makes draconian and reckless cuts to the Food and Drug Administration. FDA has long been a chronically underfunded agency, and just as Congress makes successful in reversing this disturbing trend, my Republican friends propose cutting their fiscal year 2012 budget by $285 million.

A cut of this magnitude to FDA's budget will only result in a cut in the number of personnel dedicated to reviewing device applications, a likely delay in review times, further exasperating the valid concerns of industry and patients.

Further, as Members of this Committee we have a responsibility to improve the medical device approval process not tear it down. Rushing devices to the market may help to pad the pockets of industry, but it does not keep the promise to the American public that medical devices approved by FDA will be both safe and effective.

I hope to continue to work with my colleagues to strengthen the medical device approval process and provide FDA the capacity to do so. I look forward to hearing from today's panels.

The NEW ENGLAND JOURNAL of MEDICINE

July 29, 2011

Representative Fred Upton
Chairman, Energy and Commerce Committee

Representative Cliff Stearns
Chairman, Subcommittee on Oversight and Investigations, Energy and Commerce Committee

Representative Henry A. Waxman
Ranking Member, Energy and Commerce Committee

Representative Diana DeGette
Ranking Member, Subcommittee on Oversight and Investigations, Energy and Commerce Committee

Dear Representatives Upton, Stearns, Waxman, and DeGette:

I am writing to submit an addendum to my testimony given on July 20, 2011, at a hearing of the Subcommittee on Oversight and Investigations entitled "Regulatory Reform Series #5 – FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs." I submit this addendum to provide additional information and clarification that is relevant to my testimony.

In my testimony I discussed two examples of class III (highest-risk) medical devices that had high failure rates and caused enormous harm to patients. Both of these devices (one a heart device, the other an orthopedic device) were introduced into the marketplace without pre-market clinical testing (i.e. testing in patients) sufficient to establish their efficacy or safety.

The metal-on-metal artificial hip implant, of which the DePuy ASR XL Acetabular System is a prime example, was cleared by FDA through the 510(k) process. Since the implant was judged to be substantially equivalent to a predicate device, it did not undergo clinical testing, only bench testing, prior to its introduction into clinical practice. There are 26 types of class III (highest-risk) medical devices that may still be cleared by the 510(k) pathway, which represents a huge loophole in FDA's regulatory oversight of devices. 510(k) is intended for use primarily in class II devices.

After the ASR was launched into surgical practice, it was found to fail, due to erosion of metal particles from the mobile components, at an astounding rate of 1 in 8 patients. These patients required a second operation to replace the defective implant. This unacceptably high failure rate of a device that was installed in nearly 100,000 patients resulted in a public health nightmare and an immense waste of Medicare dollars.

The second device, the Sprint Fidelis implantable defibrillator lead manufactured by Medtronic, is a critical component of a cardiac defibrillator that is designed to deliver shocks to the heart in order to restore normal heart rhythm and prevent sudden death. Unfortunately, the Sprint Fidelis lead was found to be prone to fracture, which resulted in inappropriate shocks in numerous patients and death in 13. In contrast to the metal-on-metal hip implant, the Sprint Fidelis was approved by FDA through a supplement to a previous premarket approval (PMA). The PMA process, which is specifically targeted to class III devices, is more rigorous than 510(k) clearance, and in most instances involves the submission of data from clinical trials or other careful clinical observations to establish the efficacy and safety of the product.

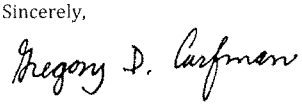
What is striking about Sprint Fidelis is that, even though it was approved by a PMA process, no clinical studies were performed in patients to ensure that the lead was safe and effective. As with the metal-on-metal hip implants, only bench testing was performed, which did not faithfully reproduce the stresses placed on the lead by actual cardiac contractions. Prior to its withdrawal from the market in 2007, it was installed in over a quarter of a million patients. FDA review of this class III device by PMA supplement was similar to a 510(k) clearance process in that it lacked clinical trials and other rigorous standards of evidence regarding safety or efficacy. This represents another large loophole in the FDA regulatory process for medical devices.

The unfortunate story of the Sprint Fidelis lead is told in greater detail in the accompanying article by Dr. William Maisel.

The FDA approval processes for these two high-risk medical devices (one by 510(k), the other by PMA supplement) were very similar in that the critical step of performing rigorous clinical studies prior to marketing was omitted. Given the technical sophistication of these complex devices, it is astounding that data from advanced clinical testing were not submitted as a central part of the approval process. In both cases, this omission had disastrous consequences for patients in the United States and around the world.

I trust that this additional information will serve to clarify these two major loopholes in device regulation. Further weakening of regulatory standards, as was suggested by some members of the Subcommittee during the hearing, will surely not be a remedy.

Sincerely,



Gregory Curfman, MD
Executive Editor
New England Journal of Medicine
Boston, Massachusetts

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

MARCH 6, 2008

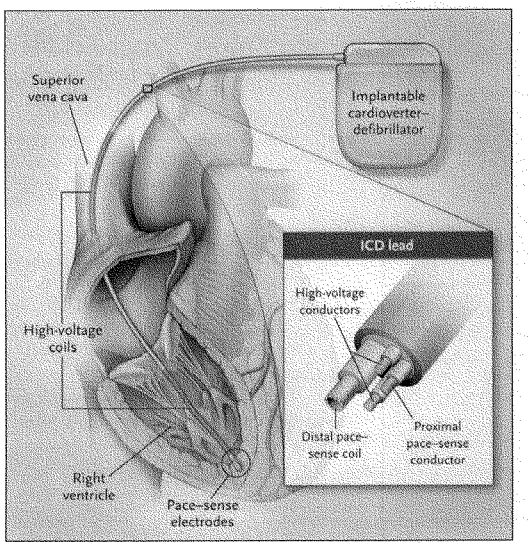
Semper Fidelis — Consumer Protection for Patients with Implanted Medical Devices

William H. Maisel, M.D., M.P.H.

When the Food and Drug Administration (FDA) approved the Medtronic Sprint Fidelis implantable cardioverter–defibrillator (ICD) lead in 2004 on the basis of bench testing but no human clinical data, there was no public outcry. Physicians rapidly incorporated the new electrode into their practice, welcoming its small diameter and ease of implantation. During the ensuing 3 years, 90% of Medtronic ICDs were implanted with this lead (see diagram). But in October 2007, after 38 months on the U.S. market and 268,000 implantations worldwide, the Fidelis was voluntarily recalled by Medtronic because of its propensity to fracture. The large number of affected patients, the billions of dollars at stake in the ICD market, and the controversy surrounding the timing of communication with physicians and patients about the lead's performance highlight the shortcomings of the regulatory system for medical devices and underscore the urgent need for legislation that will ensure adequate protection for the patients receiving them.

Obviously, no complex device can be 100% free of design, manufacturing, and performance flaws. Malfunctions inevitably occur, and manufacturers should be rewarded, not criticized, for identifying and correcting problems. The demands placed on ICD leads, in particular, are intense: they must withstand hundreds of millions of repetitive cardiac cycles, survive in the hostile environment of the human body, and allow delivery of high-voltage energy at a moment's notice. But ICD-lead fractures can result in clinically significant adverse events, including a failure to pace, a failure to defibrillate, unnecessary shocks, and death.

After concerns arose about the performance of the Fidelis, Medtronic notified physicians by letter in March 2007 of "a limited number" of physicians who were seeing a higher-than-expected rate of lead fractures. Medtronic concluded that the lead's performance was "in line with other Medtronic leads" on the basis of two main factors: analysis of returned products (though such analysis is notoriously inaccurate because most malfunctioning leads are not removed from patients and returned to the manufacturer) and a small prospective postmarketing study that found a 1.1% rate of lead failure within 2 years of implantation. Medtronic failed to note that the study — which included fewer than 100 patients followed for 2 years — was grossly un-



ICD System Consisting of a Generator and a Lead.

Cardiac signals are conducted through pace–sense electrodes from the heart to the ICD generator. Low-voltage pacing therapy, when needed, is delivered through these electrodes to treat slow heart rhythms. The high-voltage shocks required for defibrillation are delivered through high-voltage conductors. Fracture of a pace–sense electrode may result in a failure to pace or in electrical "noise" that the ICD generator may misinterpret as a fast heart rhythm, which can result in an unnecessary shock. Fracture of a high-voltage conductor could result in a failure to defibrillate.

derpowered to detect even a moderate increase in fracture rate in the Fidelis as compared with its predecessors. In short, despite implantation of the device in hundreds of thousands of patients during several years on the market, the available postmarketing data were insufficient to provide a definitive conclusion about whether there was a performance problem. Medtronic therefore began collecting and analyzing data from more than 25,000 patients participating in its remote ICD-monitoring program.

Though publicly maintaining that the lead functioned within acceptable parameters, Medtronic submitted an FDA application for design and manufacturing changes in May 2007 and, according to the FDA's public premarket approval database, received approval 2 months later. Already-manufactured leads remained on hospital shelves and continued to be implanted. By October 2007, Medtronic had confirmed the occurrence of 665 fractures in returned leads, five patient deaths to which a Fidelis lead fracture may have contributed, and a 2.3% fracture rate within 30 months of implantation (according to an analysis of the remote-monitoring data).[1] Medtronic then voluntarily recalled the product and requested the return of unused leads.

Almost immediately, numerous lawsuits were filed against Medtronic alleging personal injury, negligence in manufacturing, and failure to warn patients about the possible defects in a timely manner. In reality, manufacturers have repeatedly and knowingly sold potentially defective devices without public disclosure. For example, after identifying and correcting a design flaw that could cause premature depletion of ICD batteries, Medtronic continued to sell its inventory of potentially defective ICDs without public disclosure.[2] Similarly, the two other major ICD manufacturers, Guidant (now part of Boston Scientific) and St. Jude Medical, have knowingly marketed potentially defective arrhythmia devices unbeknownst to the public.[3,4] Often, a flawed product continues to be marketed while the manufacturer submits a revised marketing application to the FDA and awaits approval of the amended product design and manufacturing plan.

Nor is the failure to notify the public about important flaws unique to the arrhythmia-device industry. Last year, a U.S. House committee launched an investigation into whether the FDA took proper action after determining that Johnson & Johnson's Cordis unit violated laws in manufacturing its drug-coated cardiac stent. The FDA did not issue a public warning letter until several months after inspections revealed manufacturing errors, and Cordis was permitted to continue marketing the device. The failure of manufacturers and the FDA to provide the public with timely, critical information about device perfor-

mance, malfunctions, and "fixes" enables potentially defective devices to reach unwary consumers.

Some argue that public disclosure of reliability information is overwhelming and anxiety-provoking for patients. A recent editorial in the *Wall Street Journal* opined that "the real danger to public health is the overreaction to medical risk," noting that some patients refuse to have a device implanted because of concern about potential malfunctions.[5] But isn't that exactly the point — that when given information about reliability, some patients will choose not to have a device implanted? The solution is to educate patients, inform them about benefits and risks, and allow them to make their decision in consultation with their physician and family — a process called informed consent. The failure to publicly disclose adverse information about device safety subverts this process. Medtronic's president and chief executive officer, Bill Hawkins, asserts that "society's tolerance for any risks associated with medical technology is nearing zero."[5] But society is not intolerant of all risk — just unnecessary, undisclosed, and preventable risk.

According to its mission statement, the FDA is "responsible for protecting the public health" and for "helping the public get the accurate, science-based information they need." Unfortunately, the agency is failing to fulfill that mission. In 1998, the Advisory Commission on Consumer Protection and Quality in the Health Care Industry adopted a Patients' Bill of Rights whose primary tenet is that patients have "the right to receive accurate, easily understood information to assist them in making informed decisions." Regrettably, patients considering implantation of medical devices often fail to receive critical information on device safety.

The welfare of medical device recipients must become a higher priority for the FDA and manufacturers, and it is increasingly apparent that such a change will require Congressional action. Essential consumer protections are currently lacking. For example, patients with a recalled medical device are not even assured of a single visit with their health care provider at no cost to themselves (paid for by either insurance or the device manufacturer) to discuss the health implications of the recall. In addition, although FDA regulations protect human subjects participating in research studies, no such protections apply to the millions of patients who receive devices outside of clinical trials. Indeed, the vast majority of FDA approvals of medical devices occur without any representation of consumers' interests, and decisions concerning postmarket safety rarely include input from patient-advocacy groups. Meanwhile, manufacturers have an inherent financial conflict of interest when addressing device-safety issues and have stronger legal obligations to their shareholders than to the patients who use their products. This imbalance must be corrected.

The Latin motto *semper fidelis* reminds us to remain faithful to certain core principles. To protect the well-being of the recipients of medical devices and to treat them ethically, we must ensure adherence to the principles of informed consent, patient autonomy, and public disclosure of important safety information. Implanted medical devices have enriched and extended the lives of countless people, but device malfunctions and software glitches have become modern "diseases" that will continue to occur. Remarkably, we have consumer protections for airline passengers, cable-television customers, and cellular-telephone users, but few for patients who receive life-sustaining medical devices. Only with well-defined, specific consumer protections for such patients can we hope to minimize adverse health consequences and avoid costly recalls of critical medical products.

Dr. Maisel is a consultant for the FDA and a member of the Medicare Coverage Advisory Committee. The opinions expressed in this article are those of the author and do not necessarily represent the opinions, practices, policies, or positions of the FDA or the Centers for Medicare and Medicaid Services. No other potential conflict of interest relevant to this article was reported.

Dr. Maisel is the director of the Medical Device Safety Institute, Department of Medicine, Beth Israel Deaconess Medical Center, Boston.

1. Urgent medical device information: Sprint Fidelis lead patient management recommendations. Minneapolis: Medtronic, October 15, 2007. (Accessed February 14, 2008, at http://www.medtronic.com/fidelis/physician-letter.html.)
2. Reply brief for petitioner in Riegel v. Medtronic, Inc., No. 06-179 U.S. Supreme Court (November 2007). (Accessed February 14, 2008, at http://www.citizen.org/documents/riegelmeritsreply.pdf.)
3. Maisel WH. Safety issues involving medical devices: implications of recent implantable cardioverter-defibrillator malfunctions. JAMA 2005;294:955-8.
4. *Idem.* Malfunctions of implantable cardioverter defibrillators. JAMA 2006;295:161-2.
5. Stopping medicine's machines. Wall Street Journal. January 2, 2008:A10. (Accessed February 14, 2008, at http://online.wsj.com/article_email/SB119923693299961231-lMyQjAxMDE4OTA5MjIwMzI2Wj.html.)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NOV 29 2011

The Honorable Cliff Stearns
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Chairman:

Thank you for providing the opportunity for the Food and Drug Administration (FDA or the Agency) to testify at your Subcommittee's July 20, 2011, hearing entitled "Regulatory Reform Series #5 – FDA Medical Device Regulation: Impact on American Patients, Innovation and Jobs." This letter provides responses for the record to questions posed by certain Members of the Subcommittee in your letter of August 9, 2011.

If you have further questions, please let us know.

Sincerely,

Jeanne Ireland
Assistant Commissioner
for Legislation

cc: The Honorable Diana DeGette
Ranking Member
Subcommittee on Oversight and Investigations

We have restated each of the Members' questions below in bold, followed by our responses.

The Honorable Cliff Stearns

1. **Dr. Shuren, in your testimony you stated that there is no device lag between Europe and the United States. In addition, an August 1, 2011 op-ed in the WSJ by Commissioner Hamburg stated, "FDA consistently approves the vast majority of priority drugs and medical devices as fast as, or faster than, our European counterparts." The op-ed went on to state, "all 23 cancer drugs approved by both agencies during this period were marketed first in the U.S." However, in Dr. Sean Ianchulev's testimony, he stated, "I reviewed all approved PMAs of medical devices in the ophthalmic field over the last 5 years listed on the FDA website as an indicator of most major innovations in my specialty. These represent all the pioneering innovations made available to me as an eye surgeon through the more rigorous PMA path in the United States. The results were informative: of all 12 device approvals, all (100%) were already approved and available for use outside the U.S. in the EU and in as many as 20-40 countries. In addition, some of the devices already had vast clinical experience dwarfing the FDA clinical trial numbers – in some examples more than 100,000 worldwide patients had been treated prior to the FDA approval."**

   Please provide the committee a list of all the PMA approved medical devices from 2008-today that are not yet available in Europe.

Dr. Shuren's testimony from the July 20, 2011, hearing states, "In terms of time to market, data show that the United States is performing as well or better than the European Union (EU). An industry-sponsored analysis[1] shows that low-risk 510(k) devices without clinical data (80 percent of all devices reviewed each year) came on the market first in the United States as often as or more often than in the EU. The EU typically approves higher-risk devices faster than the United States because, unlike in the United States, the EU does not require the manufacturer to demonstrate that the device actually benefits patients."

Dr. Hamburg's op-ed in the *Wall Street Journal* stating that FDA consistently approves the vast majority of priority drugs and medical devices as fast as, or faster than, our European counterparts is consistent with Dr. Shuren's statement about medical device approvals. In addition, with regard to drug approvals, in a report released on November 3, 2011, entitled "FY 2011 Innovative Drug Approvals," FDA provides details of how the Agency used expedited approval authorities, flexibility in clinical trial requirements, and resources collected under the Prescription Drug User Fee Act (PDUFA) to boost the number of innovative drug approvals to 35 for the fiscal year (FY) ending September 30, 2011. The report also shows faster approval times in the United States when compared to FDA's counterparts around the globe. Twenty-four of the 35 approvals occurred in the United States before any other country in the world, and also

[1] California Healthcare Institute and The Boston Consulting Group, "Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry" (February 2011), available at *http://www.bdg.com/documents/file72060.pdf.*

before the EU, continuing a trend of the United States leading the world in first- approvals of new medicines.

You also request a list of all medical devices approved through the premarket approval (PMA) process from 2008 to present that are available in the United States but not in the EU. We are not aware of any comprehensive database that contains information related to device status in the EU. It is difficult to track medical device approvals or other important data in the EU since there are few to no publicly accessible, centralized systems for collecting and monitoring information about medical device approvals or safety problems in the EU. Manufacturers use "Notified Bodies," which are private, non-governmental entities that review and approve devices by giving them a "CE Marking" (Conformité Européene or European Conformity). These decisions are kept confidential and are not released to the public or to EU regulatory bodies.

The Honorable Michael C. Burgess

1. **Dr. Shuren, I've heard you say previously that FDA is meeting its user fee goals for 95% of submissions. But when I look at these charts from the most recent "Quarterly Update on Medical Device Performance Goals," dated May 4, 2011, there are an awful lot more goals than 5% that are not being met. I know that 510(k) submissions account for about 95% of the device reviews that FDA does each year, but all of these red boxes where FDA is not meeting its user fee goals are very concerning to me. I also note that the goals that aren't being met are largely the premarket approval goals, and as you know, these are the most cutting-edge, breakthrough technologies. What are you doing—right now—to rectify this situation?**

FDA is meeting or exceeding goals agreed to by FDA and industry under MDUFA II for approximately 95 percent of the submissions we review each year. The limited goals which are not being met include Original Premarket Approval (PMA) Tier II goals, Modular PMA Tier I goals, and 180-day PMA supplement Tier II goals. PMA submission goals have not been met because of a combination of factors, including increasing workload, staff turnover, and growing device complexity.

FDA's Center for Devices and Radiological Health (CDRH or the Center) has undertaken a number of steps to address these issues, including: drafting clinical trials guidance, identifying and recruiting needed staff expertise, strengthening its external-expert program, and undertaking evaluation of its premarket IT systems. These steps include:

- Improving communication between FDA and industry through enhancements to interactive review (some of these enhancements will be in place by the end of 2011);
- Issuing guidance clarifying the criteria used to make benefit-risk determinations a part of device premarket review. This will provide greater predictability and consistency and apply a more patient-centric approach by considering patients' tolerance for risk in appropriate cases (draft guidance issued August 15, 2011);
- Creating standard operating procedures for when a reviewer can request additional information regarding a premarket submission, and identifying at what management level

the decision must be made. These steps are intended to provide greater predictability, consistency, and the appropriate application of the least-burdensome principle by reducing the number of inappropriate information requests (Draft Standard Operating Procedures issued November 10, 2011);

- Developing a range of updated and new guidances to clarify CDRH requirements for predictable, timely, and consistent product review, including device-specific guidance in several areas such as mobile applications (draft guidance released July 19, 2011) and artificial pancreas systems (draft to be issued in December 2011);
- Revamping the guidance development process through a new tracking system, streamlined processes, and, to the greatest extent possible with available resources, supplementing core staff to oversee the timely drafting and clearance of documents (to be completed by the end of 2011);
- Streamlining the clinical trial Investigational Device Exemption (IDE) processes by providing industry with guidance to clarify the criteria for approving clinical trials and the criteria for when a first-in-human study can be conducted earlier during device development (draft guidances issued November 10, 2011). IDEs are required before device testing in humans that involves significant risks may begin, and they ensure that the rights of human subjects are protected while data on the safety and efficacy of medical products are being gathered. These actions aim to create incentives to bring new technologies to the United States first:
- Implementing internal business process improvements to ensure that decisions are made by the appropriate level of management, that decisions are made consistently and efficiently, and that we appropriately apply the least-burdensome principle. For example, CDRH created the internal Center Science Council to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decision-making (Center Science Council draft charter published March 31, 2011);
- Creating a Network of Experts to help the Center resolve complex scientific issues, which will ultimately result in more timely reviews. This network will be especially helpful as FDA confronts new technologies (Draft Standard Operating Procedures issued September 30, 2011);
- Instituting a mandatory Reviewer Certification Program for new reviewers (program launched September 2011);
- Instituting a pilot Experiential Learning Program to provide review staff with real-world training experience as they participate in visits to manufacturers, research and health care facilities, and academia (to begin in early 2012);
- Providing industry with specific guidance on how to ensure the quality and performance of clinical trials while taking the least-burdensome approach, so that industry conducts studies that are more likely to support the approval of their products (draft guidance released August 15, 2011);
- Streamlining the *de novo* review process, the pathway by which novel, lower-risk devices without a predicate can come to market (draft guidance released October 3, 2011); and
- Implementing a Corrective and Preventive Actions (CAPA) system for premarket review to identify, track, and correct or prevent problems. On October 1, 2011, the Center started a pilot of the CAPA system in the CDRH Office of Device Evaluation (ODE).

2. In 2010, FDA granted 19 premarket approvals, down from 48 in 2000. What steps are you taking to ensure that patients have access to cutting-edge medical technology?

The numbers of original PMA approvals from year to year can vary significantly, as the number of original PMA applications FDA receives annually can vary significantly. Since the total numbers of original PMAs submitted annually (40–60) is small compared to 510(k)s (3000–4000), variations from year to year appear more dramatic. Changes in economic conditions, among other things, affect the ability of companies to finance research and development and market new products. In addition, in 2002–2003, the Center created the Office of In Vitro Diagnostics, consolidating functions and staff from other CDRH offices, including ODE. An accurate comparison would have to reflect the combined original PMAs approved by both offices each year.

Finally, the number you are quoting for 2010 is preliminary, as the receipt cohort for that year is not closed. In other words, some original PMA applications from 2010 are still pending. In addition, when examining PMA trends, it is important to look to "PMA-related submissions," rather than just original PMAs. Under the medical device user fee program, FDA tracks "PMA-related submissions" for a more accurate assessment of workload. These include original PMAs and PMA supplements, or modifications to original PMAs. PMA supplements are submitted when a sponsor wants to, among other things, add indications; change performance or design specifications, circuits, components, ingredients, principles of operation, or physical layout of the device; change manufacturing facilities, methods, or quality control procedures; or change sterilization procedures. Increases in the number of PMA-related submissions from 2004 to 2010 (approximately 50 percent, from 3,051 to over 5,100) account for the greatest increase in workload for the device review program. FDA is taking steps under the Action Plan to facilitate patients' access to cutting edge medical technology. Specific steps that we are taking include:

- Issuing guidance clarifying the criteria used to make benefit-risk determinations a part of device premarket decisions. This will provide greater predictability and consistency and apply a more patient-centric approach by considering patients' tolerance for risk in appropriate cases (draft guidance issued August 15, 2011);
- Creating standard operating procedures for when a reviewer can request additional information regarding a premarket submission and identifying at what management level the decision must be made. These steps are intended to provide greater predictability, consistency, and the appropriate application of the least-burdensome principle by reducing the number of inappropriate information requests (Standard Operating Procedures issued November 10, 2011);
- Developing a range of updated and new guidances to clarify CDRH requirements for predictable, timely, and consistent product review, including device-specific guidance in several areas such as mobile applications (draft guidance released July 19, 2011) and artificial pancreas systems (to be completed by the end of 2011);
- Revamping the guidance development process through a new tracking system, streamlined processes, and, to the greatest extent possible within available resources, core staff to oversee the timely drafting and clearance of documents (to be completed by the end of 2011);

- Streamlining the clinical trial IDE processes by providing industry with guidance to clarify the criteria for approving clinical trials, and the criteria for when a first-in-human study can be conducted earlier during device development. (IDEs are required before device testing in humans that involve significant risks may begin, and they ensure that the rights of human subjects are protected while gathering data on the safety and efficacy of medical products.) These actions aim to create incentives to bring new technologies to the United States first (guidances issued November 10, 2011);
- Implementing internal business process improvements to ensure that decisions are made by the appropriate level of management, that decisions are made consistently and efficiently, and that we appropriately apply the least-burdensome principle. For example, CDRH created the internal Center Science Council to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decision-making (Center Science Council established March 31, 2011);
- Creating a network of experts to help the Center resolve complex scientific issues, which will ultimately result in more timely reviews. This network will be especially helpful as FDA confronts new technologies (Standard Operating Procedures issued September 30, 2011);
- Instituting a pilot Experiential Learning Program to provide review staff with real-world training experiences as they participate in visits to manufacturers, research, and health care facilities, and academia (to begin in early 2012);
- Providing industry with specific guidance on how to ensure the quality and performance of clinical trials while applying the least-burdensome principle, so that industry conducts studies that are more likely to support the approval of their products (guidance released August 15, 2011); and
- Streamlining the *de novo* review process, the pathway by which novel, lower-risk devices without a predicate can come to market (draft guidance released October 3, 2011).

3. In this performance report, FDA reports meeting its 510(k) goals for 2008 submissions. Why has FDA not reported performance on submissions from 2009 and 2010? When will this information be available?

Data on device review performance in FY 2009 and 2010 are publicly available on FDA's website (see MDUFA quarterly and annual performance reports, available at *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm109210.htm*; however, the data set for a fiscal year is not complete until a final decision is rendered on each application in the receipt cohort for that fiscal year. Therefore, we project best- and worst-case performance to guide us in managing and reporting on performance. Receipt cohorts can remain open for two years for various reasons, e.g., submissions that required more than one interaction with the submitter.

In accordance with the MDUFA II commitment letter, as outlined in our agreement with industry, performance for each goal is measured by the receipt cohort (applications received) for each fiscal year. The 510(k) Tier I performance goal for FY 2009 and FY 2010 is a decision for 90 percent of applications within 90 days. At the time of the May 4, 2011, quarterly update, the FY 2009 and FY 2010 510(k) receipt cohorts still had submissions that had not received a final

decision as of March 31, 2011. Therefore, we indicated best- and worst-case performance projections for each fiscal year. Best- and worst-case performance projections for the 510(k) Tier I goal were 90 percent and 89 percent, respectively, for FY 2009, and 93 percent and 79 percent, respectively, for FY 2010.

During the July 16, 2011, quarterly update, the FY 2009 cohort was sufficiently complete to determine that the Agency had met its Tier I performance goal of 90 percent. For FY 2010, the best- and worst-case performance projections were 92 percent and 86 percent, respectively.

4. **My understanding is that with the FDA reorganization Dr. Hamburg has put in some people to coordinate communication between centers – can you explain how this has worked in your eyes?**

Commissioner of Food and Drugs, Dr. Margaret Hamburg, announced the restructuring of the FDA Office of the Commissioner on July 13, 2011. The new organizational alignments more accurately reflect the Agency's responsibilities, subject matter expertise, and mandates in an ever-more-complex world, where products and services do not fit into a single category. The most obvious change is that the Agency's programs, in terms of a reporting chain to the Commissioner, have been divided into "directorates" that reflect the core functions and responsibilities of the Agency. This new management structure is intended to enable the Office of the Commissioner to better support the Agency's core scientific and regulatory functions, and help tie together programs that share regulatory and scientific foundations.

As part of this restructuring, Dr. Hamburg established a new position of Deputy Commissioner for Medical Products and Tobacco to provide high-level coordination and leadership across the Centers for drug, biologics, medical devices, and tobacco products. The new Office of Medical Products and Tobacco (OMPT) is comprised of those four Centers (which previously reported directly to the Commissioner): the Center for Devices and Radiological Health (CDRH), the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Tobacco Products (CTP). The new OMPT also oversees the Office of Special Medical Programs, which contains four Offices that were previously in the Office of the Commissioner: the Office of Orphan Product Development, the Office of Pediatric Therapeutics, the Office of Combination Products, and the Office of Good Clinical Practice.

Dr. Stephen Spielberg, former Dean of Dartmouth Medical School and Director of the Center for Personalized Medicine and Therapeutic Innovation at Children's Mercy Hospital in Kansas City, accepted the position of Deputy Commissioner for OMPT when the restructuring of the Commissioner's Office was announced last July. Dr. Spielberg now has direct-line authority over the four medical product Centers and the special medical programs and, as such, will provide advice and counsel to the Commissioner on all FDA medical product and tobacco-related programs and issues. However, the Centers themselves remain unchanged in this reorganization—each of the Centers, including CDRH, remains as a discrete management entity under its own leadership.

5. **For 510(k) performance, FDA has also reported that the average total time to 510(k) decision is increasing and the average number of review cycles per submission is**

increasing. What steps are you taking to identify why the total time to 510(k) decisions is increasing?

The MDUFA II goals agreed to by industry and FDA measure FDA review days, not the days that submitters take to respond to outstanding issues in their submissions. Overall, FDA performance is strong in meeting those goals, even in the face of a growing overall workload and the growing complexity of medical devices.

However, the total time to a decision (FDA review time plus the time it takes a sponsor to provide requested information) has increased. FDA bears some responsibility for the increase in approval times and has been instituting management changes. As a result, in 2010, total time for 510(k)s appears to have stabilized, and preliminary data suggest that the total time for PMA decisions is improving. Industry also bears some responsibility for the increase in overall time to decision. FDA recently conducted an analysis of premarket review times under the 510(k) program and identified quality issues in more than 50 percent of 510(k) applications. These quality issues require Agency staff to prepare and issue additional information (AI) letters, resulting in additional review cycles.

For our part, after conducting a thorough assessment of the 510(k) review program and an assessment of how CDRH uses science in regulatory decision-making, we issued two reports in August 2010 which found that we had not done as good a job managing our premarket review programs as we should have and that we needed to take several critical actions to improve the predictability, consistency, and transparency of these programs.

We found, for example, that we have new reviewers who need better training. We need to improve management oversight and standard operating procedures. We need to provide greater clarity for our staff and for industry through guidance about key parts of our premarket review and clinical trial programs and how we make benefit-risk determinations. We need to provide greater clarity for industry through guidance and greater interactions about what we need from them to facilitate more efficient, predictable reviews. We need to make greater use of outside experts who understand cutting-edge technologies, and we need to find the means to handle the ever-increasing workload and reduce staff and manager turnover, which is almost double that of FDA's drugs and biologics Centers.

The Agency solicited public comment on the recommendations identified in the studies and received a range of perspectives from stakeholders, including medical device companies, industry representatives, venture capitalists, health care professional organizations, third-party payers, patient and consumer advocacy groups, foreign regulatory bodies, and others. After considering the public input, in January 2011, FDA announced 25 specific actions that the Agency would take this year to improve the predictability, consistency, and transparency of our premarket review programs. These actions are described in the answer to Question #1.

Finally, FDA needs adequate, stable funding to manage a device program that can move safe and effective products to market without delay. Reauthorizing MDUFA in a timely fashion and at a sufficient level is crucial.

6. **Earlier this year the Wall Street Journal and other publications reported on a manufacturer that appealed the denial of a PMA application for a new technology that has the potential to benefit colonoscopy patients; I might add, it is a technology that was recommended for approval by an FDA independent Advisory Panel and is approved by regulatory authorities in Canada, Europe and Australia. It was further reported that FDA granted the manufacturer's appeal in November of 2010, eight months after the manufacturer filed their request, and as of today they haven't had a second panel hearing yet. As I understand it, little progress has been made since November. I also note from FDA's public docket, that FDA has declined the manufacturer's request to even meet to discuss the appeal process. Aren't these lengthy delays, and use of such avoidance tactics, in-effect denial of due process?**

7. **When FDA takes months to award an appeal, then takes little action for another 9 months, it sends the wrong message to patients, manufacturers, inventors and investors, all of whom want and deserve a responsive agency. Do you think months of non-action and a lack of communication are appropriate ways of doing business?**

We believe that you are referring to SEDASYS®, an integrated patient monitoring and drug delivery system; the device's proposed indication is for the intravenous administration of 1 percent propofol injectable emulsion for the initiation and maintenance of minimal-to-moderate sedation in adult patients undergoing colonoscopy and esophagogastroduodenoscopy (EGD) procedures. Ethicon Endo-Surgery Inc. (EES) submitted a PMA for SEDASYS in 2008. In February 2010, CDRH issued a letter to EES indicating that the PMA for SEDASYS was not approvable because CDRH concluded that the data and information offered in support of the PMA did not provide a reasonable assurance that the device is safe under the conditions of use prescribed, recommended, or suggested in the proposed labeling. On March 25, 2010, EES requested review of the Not-Approvable Letter under section 515(g)(2) of the FD&C Act.

FDA's goal is to resolve disputes fairly and expeditiously. When EES appealed CDRH's Not-Approvable Letter in March 2010, the next step in the process was a formal denial of the PMA. FDA held off taking that step because EES indicated an interest in continuing discussions with CDRH about how and whether the PMA could still be granted approval. When the discussions between EES and CDRH did not prove fruitful, CDRH issued a formal denial of the PMA in October 2010. Shortly thereafter, the Office of the Commissioner granted the sponsor's petition for review of the order denying the PMA and began the process for referring the PMA, and the basis for the order denying its approval, to the Medical Devices Dispute Resolution Panel (MDDRP). At that time, the Office of the Commissioner made clear that FDA would be observing separation of functions and that, as a result, the Office of the Commissioner would not engage in *ex parte* communications with either EES or CDRH. As the docket at *www.regulations.gov* reflects (No. FDA-2010-P-0176), however, the Office of the Commissioner has been in frequent communication with both parties about each step of the process since granting the petition for review. The Office of the Commissioner ultimately scheduled the MDDRP meeting for December 14, 2011, to discuss SEDASYS.

By letter dated November 28, 2011, EES notified the Office of the Commissioner that it was withdrawing its appeal. The Office of the Commissioner is therefore cancelling the meeting

scheduled for December 14, 2011. CDRH and EES have agreed upon a path forward for continued review of the application.

For additional information about the Agency's review of the SEDASYS® system, please see *http://www.gpo.gov/fdsys/pkg/FR-2011-11-21/html/2011-29888.htm.*

8. What is ultimately the impact to <u>patients</u> and what can be done to rectify this situation?

As the docket reflects, CDRH had a number of concerns that go to the safety of the SEDASYS device. The administration of anesthesia can present significant risks to patients. Consistent with the statutory provision under which EES sought review, the process followed by OC was intended to resolve the disagreement between CDRH and EES with respect to those concerns.

<u>The Honorable Brian Bilbray</u>

1. When did you become aware that employees of the Center for Devices and Radiological Health (CDRH) wrongfully denied MELA Sciences an advisory panel review for its MELAFind PMA? What did you do upon becoming aware of this information?

CDRH should have granted MELA Sciences an advisory panel meeting on this first-of-a-kind PMA upon MELA Sciences' request. The decision to go to panel is embedded in the review process. When we have outstanding issues in reviewing an application that need to be addressed, we typically issue a major deficiency letter; then we would go to panel. Here, we incorrectly issued the Not-Approvable Letter without first holding an advisory panel meeting as requested by MELA Sciences. The panel meeting should have occurred first since the panel had not weighed in on this type of device before. In response to a second request for an advisory panel meeting by MELA Sciences after we issued the Not-Approvable Letter, we scheduled an advisory panel that met on November 18, 2010, to review and make a recommendation regarding this PMA. The panel voted 8 to 7 in favor of the PMA's risk-benefit profile. To ensure that a similar circumstance does not occur again, we have clarified our policies and procedures with each of CDRH's Divisions involved in the review of PMAs.

2. We understand that through counsel MELA Sciences requested in writing a retraction of the March 10, 2010 not approvable letter. Why did you not immediately retract the not approvable letter? Why did it take you 15 months to acknowledge CDRH's illegal denial of MELA Sciences' right to an advisory panel review of its PMA?

The Not-Approvable Letter raised issues that required resolution for the application to be considered approvable. A Not-Approvable Letter is not considered a denial by the Agency. It is a letter that indicates what the manufacturer needs to provide to place the application in approvable form. Subsequent submissions respond to the Not-Approvable Letter, including the submission with additional information that was the basis for the approvable decision and approval decisions that the Agency has rendered. There was no justification for retraction of the Not-Approvable Letter. In order to go to panel, the application needed additional information to

present to that panel. The Agency often works with sponsors to ensure that applications are in the best form possible to present to the advisory committee. If there are a number of outstanding issues related to the application, it may cloud the vote at the panel meeting. Therefore, by requesting additional information, the Agency resolves many of these issues, leaving the advisory committee to a much smaller subset of issues, if any remain at all. Advisory committee meetings are held when both the sponsor and FDA are prepared to have an advisory committee meeting.

3. **On November 18, 2010, FDA's CDRH presented a slide presentation to the General and Plastic Surgery Devices Panel concerning the MELAFind PMA. Did the agency ever post on its website its original slide presentation? Why did FDA post on its website revised slides on July 19, 2011, the day before this Congressional hearing? What were the changes to the slides? Who authorized the changes to the slides and their posting on the website? Has anything else changed on FDA's website regarding the MELAFind advisory panel meeting?**

It is clear from our review of this situation that staff made editorial revisions to the slides to consolidate information. Although the final slide presentation did not provide the correct definition of effectiveness, the FDA presenter corrected this error verbally during the meeting (see page 101 of the transcript of the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee Meeting Notice available at *http://www.fda.gov/AdvisoryCommittees/Calendar/ucm223189.htm.*) It also should be noted that the correct definitions were read to the panel members prior to voting, as is standard practice at advisory committee meetings. We have since implemented an additional slide review by our regulatory advisor staff prior to FDA slide presentations of regulatory materials to advisory panels so that we may catch editing errors prior to a presentation.

The original slide presentation was provided to the public at the meeting, but was not posted immediately afterward. The slides were revised due to the sponsor's concern about the wording on the one slide, which was stated clearly at the meeting and addressed in the transcript. The review team made changes to two slides based on feedback given at the meeting. CDRH did not want an editorial error to continue to be displayed and create confusion. The slides were updated on the website with a notation to the edits that were made.

4. **I understand that at the advisory panel meeting your staff incorrectly instructed the panel members on the FDA regulations' directions on how to determine a device's safety and effectiveness. Specifically, your staff purportedly showed a safety determination regulation that quoted and incorporated the key portion of the device effectiveness regulation, and then created an effectiveness determination standard that is foreign to the agency's actual effectiveness determination regulation. I have entered into the record the slide that FDA presented to the panel on determining safety and effectiveness and the slide that MELA presented that quotes the actual language from FDA's regulations. When did you become aware of this inappropriate CDRH conduct? What action did you take to address this conduct? What action did you take to ensure that review teams do not mislead advisory panels in this way again?**

On investigation, this was not a conduct issue, but rather an error made during consolidation of the slide presentation. The original presentation was too long and an attempt to consolidate the slides resulted in having text merged incorrectly. The mistake was corrected during the presentation at the meeting by the speaker as well as having been pointed out by the sponsor.

5. **CDRH representatives created and presented a slide to the MELAFind advisory panel that informed the panel that "[it] will not be asked to address whether the sponsor had met the items of the protocol agreement...." What is the purpose of a protocol agreement that stipulates the criteria of safety and effectiveness if the CDRH staff essentially instructs the panel to ignore whether the stipulated endpoints have been met?**

Every PMA product under review needs to be assessed regarding safety and effectiveness based on the data obtained from clinical trials to assess its risk vs. benefit for use in the U.S. population. A protocol agreement is designed to allow agreement with regard to the conduct of a specific protocol that then results in data to be submitted in a PMA for review by the Agency. These results of the study must be evaluated to ensure that reasonable assurance of safety and effectiveness has been established. As an example, if the protocol was agreed to and adhered to by the sponsor but the trial unfortunately was not a success and the device failed to meet its primary endpoint, it would not likely result in an approval. The review of the data generated from a study establishes the risk/benefit profile, the indication for use of the device, as well as informs the final device labeling for the safe and effective use of the device. In this case, the advisory panel weighed in and recommended changes, such as a limitation that the product should only be indicated for use by trained dermatologists who can appropriately determine which lesions and patients would benefit from MELAFind use, and they further recommended the development of a training program. MELA Sciences submitted a revision to the indications for use to restrict the device to use by dermatologists, along with plans for a training program. This additional information adequately addressed many of the issues raised in the Not-Approvable Letter and raised by the panel, and led to further Agency discussions with the applicant and ultimately the issuance of the Approval Letter on November 1, 2011.

6. **There are significant new medical technologies, such as whole genome sequencing, whole-transcriptome sequencing, and new epigenomics and proteomics modalities that have the potential to have major positive impacts on the diagnosis of diseases. In fact, some of these innovations have led to jobs in my hometown of San Diego. How have you prepared the Center to deal with these new technologies? How have you changed your application requirements or reviews?**

The Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD) in CDRH is at the forefront of technology changes in the area of *in vitro* diagnostics, such as having written the first guidances on genetic testing in clinical laboratories and multiplex genetic testing, as well as a number of other FDA guidances (see the examples of some of the FDA-issued guidances below). OIVD has a long history of flexibility in approach to novel technologies and applications, as can be witnessed by the number of approved *de novo* applications for assays performance, which easily can be accessed through FDA's public data base of all cleared or approved diagnostic tests (*http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm*).

A testimony to OIVD's flexibility was the clearance of the first genomic "chip"-based assay in which OIVD cleared Roche's Amplichip (a drug metabolizing enzyme genotyping system) in less than a week of FDA review time.

More recently, FDA has been working on new medical technologies, such as cytogenetic arrays (array CGH, SNP arrays) and personalized medicine—where recently FDA approved two drugs and their companion diagnostics (Zelboraf-BRAF V600 Mutation Test, and Xalkori-ALK Break Apart FISH Prove Kit). FDA's engagement in facilitating and developing new approaches, while at the same time looking for public input and maintaining transparency, is apparent in the number of recently held public meetings. For example:

- Advancing Regulatory Science for Highly Multiplexed Microbiology/MCM Devices public meeting (10/13/11)
- Array-Based Cytogenetic Tests: Questions on Performance Evaluation, Result Reporting and Interpretation (6/30/10)
- Public Meeting: Incorporation of New Science Into Regulatory Decision-Making Within the CDRH (2/9/10).

The discussions at the public meeting on array-based cytogenetic tests resulted in a proposed novel approach to cytogenetic array validation used to detect chromosomal abnormalities in the DNA of a patient as an aid to diagnose genetic cause of mental retardation, developmental delay, and multiple congenital abnormalities. This approach includes selection and validation of an appropriate and adequate subset of genetic markers, with an inference that the platform/test as a whole is analytically valid; clinical interpretation should rely on the appropriately certified professionals.

Some FDA-issued guidance documents relevant to genetic testing are:

- Guidance on Pharmacogenetic Tests and Genetic Tests for Heritable Markers *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071075.pdf*
- Class II Special Controls Guidance Document: CFTR Gene Mutation Detection Systems *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071104.pdf*
- Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Genotyping System - Guidance for Industry and FDA Staff
- *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071085.pdf*
- Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems - Guidance for Industry and FDA Staff *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071061.pdf*

There is enormous growth in next-generation sequencing (NGS) platform development. In parallel, new iterations of sample preparation part (pre-NGS instrument) and bioinformatics tools are continuously being developed by different companies and academic centers. Some of the

common applications include resequencing the whole genome to varying degrees of coverage, using hybridization-capture techniques to resequence a targeted subset (such as the protein coding sequences in exome sequencing), analyzing chromatin modification and protein binding that can be mapped by chromatin immuno-precipitation sequencing (ChIP-Seq), employing massively parallel sequencing to create 'epigenomic maps,' and sequencing RNA transcripts (RNA-Seq) to count their abundance or identify novel splice forms.

Some of the NGS is already starting to be used clinically, for very specific and limited applications, by highly trained labs with appropriate expertise, and a follow-up result confirmation and validation. One of the ultimate goals may be sequencing becoming so simple and inexpensive that whole genome sequencing (WGS) can be deployed routinely throughout biomedicine.

FDA ultimately has to balance public safety concerns with the goal of fostering innovation and enabling the translation of these new technologies to benefit public health. With the emergence of these novel technologies, FDA must prepare for new regulatory challenges while continuing to apply scientific evidence-based regulatory oversight. One of the first questions is to understand how to analytically evaluate the WGS data generated by the emerging NGS techniques. To this end, as FDA endeavors to develop evaluation protocols and standards, we are working with other federal partners, including the National Center for Biotechnology and the National Human Genome Research Institute, both parts of the National Institutes of Health (NIH), as well as the National Institute of Standards and Technology.

In June 2011, FDA hosted a public meeting entitled Ultra-High Throughput Sequencing for Clinical Diagnostic Applications in order to open the dialog between experts in the field, looking into standardizing requirements for analytical validation and bioinformatics questions. Discussions included developing reproducible and transparent evaluation protocols adaptable to accommodate emerging NGS technologies for a variety of clinical uses, while elucidating advantages and pitfalls of any particular platform, sample preparation method, or bioinformatics tool. This would enable the end users to better understand the performance of any particular platform and to select the appropriate method for their specific application. This meeting exposed many questions and uncertainties related to rapid evolution and development on novel and potentially better methodologies and platforms. One of the outcomes of the meeting was a suggestion that there may be a need to build a coalition, likely involving academia, device manufacturers, software developers, and clinical laboratory end users, to collectively develop some ways of standardization.

FDA is proactively participating with other federal partners in building the regulatory path for emerging new technologies such as Ultra-High Throughput Sequencing for WGS analysis to facilitate the translation of novel technology into clinical practice. Some suggestions for the way forward include placing next generation sequencing platforms used in clinical applications under Quality System, to make sure they are produced and perform consistently, and providing or selecting specific standards that can be used to evaluate performance of the whole system, starting from pre-analytical phase (e.g. library preparation, sample preparation, etc), through sequencing platform, to bioinformatics used to provide results. In parallel, FDA is continuing to work with platform manufacturers to establish a flexible and transparent way to accomplish this,

while simultaneously assuring that devices used are safe and effective for use in clinical applications.

For proteomics, FDA is partnering with researchers in exploring the regulatory landscape. In coordination with the American Association of Clinical Chemistry and NIH, mock 510(k)s were developed and reviewed by the Agency. As a result, the submissions and the FDA review were published in order for investigators in the field and FDA to work out what issues need to be addressed so that, in the future, there can be a successful submission.

The Honorable Marsha Blackburn

1. **My question relates to the consistent application of regulatory standards and maintaining a level playing field for all manufacturers. Currently, the criteria demanded by CDRH to evaluate new medical devices in a specific product class can seem arbitrary to manufacturers. The criteria often are inconsistent with FDA precedent for similar devices, and changes in the criteria are not scientifically justified by CDRH. This has become a noticeable trend during the last two years.**

   More specifically, CDRH appears to be applying clinical trial success requirements that are significantly different with respect to primary and secondary endpoints from those that have been used to evaluate and approve other products, even those approved within the past 18 months. The application of new standards for approvability of similar products that exceed the standards applied to contemporary approvals negatively impact both patients and jobs while also increasing healthcare costs by limiting competition.

   Please comment on the regulatory process and statutory standards at CDRH that allow review teams to arbitrarily (no scientific or regulatory standard basis) apply different criteria to the new products of a given class that are far above those criteria used to approve similar device types that have been recently (within the past 18 months) reviewed by an FDA Advisory Panel and approved by the FDA.

Consistent with the requirements for 510(k) submissions, FDA may require clinical data when a firm seeks a new indication for use or where there are differences in the technological characteristics between the firm's device and its predicate that could affect safety or effectiveness. FDA asks for clinical studies in only eight to ten percent of 510(k) submissions, and often the requested studies are simple and small. For example, FDA recommends that for pulse oximeters—medical devices that indirectly monitor the oxygen saturation of a patient's blood—clinical data be collected from as few as 10 patients. In addition, for establishing clinical data in support of a 510(k) application, the Agency recognizes a standard set by the Association for the Advancement of Medical Instrumentation, which requires a validation study consisting of as few as 35 subjects for which clinical data are required. Consistent with statutory requirements, all PMAs contain clinical data.

The Agency has no data to suggest that, as a general matter, FDA has demanded larger, more extensive clinical trials in the past five years for 510(k)s or PMAs. Clinical studies are tailored to the type of device and the specific questions that need to be addressed. That is not to say that FDA demands full knowledge and understanding of long-term risks and performance before it will approve a device for marketing. For PMA devices, the Agency increasingly uses its authority to require post-approval studies to answer important, specific questions regarding device performance after the device has been approved for marketing. For example, if there are questions about long-term durability of an implanted device, the Agency may allow the device to be marketed while further data collection continues to address that issue.

Whenever possible, FDA seeks to minimize clinical trial or preclinical requirements when scientific knowledge suggests that this is appropriate. For example, establishing the safety and effectiveness of a first-generation drug-eluting stent (DES) required extensive preclinical testing programs and clinical studies. However, the fundamental work performed to gain initial approval of first-generation DES devices has been successfully leveraged by several DES manufacturers to decrease clinical trial requirements for next-generation stents, which typically incorporate modest changes to the first-generation design.

More specifically, FDA reviewers concluded that a single-arm clinical trial (rather than a randomized controlled study) would be an acceptable design for the pivotal IDE trials of the Boston Scientific TAXUS® Liberte™, Abbott XIENCE Prime™, and Medtronic Resolute® next-generation DES. The reason CDRH permitted this approach is that these devices represent iterations of prior DES, in which a component of the combination product has been modified (e.g., a polymer coating or stent platform). This was acceptable based on our analysis of the comprehensive preclinical and clinical data generated from the prior-generation DES, and demonstrates the Agency's flexibility and willingness to tailor data requirements when appropriate.

Another example is the total artificial hip. CeramTec purchased the rights to the Wright Medical TRANSCEND® ceramic-on-ceramic total artificial hip clinical data set and approved PMA. Because the articulating surfaces of the components are all manufactured by CeramTec, FDA allowed manufacturers to use preclinical testing to leverage the Wright Medical TRANSCEND® data set. Five manufacturers had their PMAs approved, referencing the TRANSCEND® clinical data set with a condition of approval to conduct a post-approval study in a new cohort of patients.

This sometimes works in the other direction, too, in that information gleaned from competitor application reviews and post-market studies may bring to light information that changes the risk-benefit analysis and causes the Agency to look more critically at the next submission in a product category. This is appropriate. The reasons for it cannot always be shared with applicants due to statutory confidentiality requirements, possibly causing the Agency to appear arbitrary.

Under the 510(k) Action Plan, we have established an internal Center Science Council to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decision-making. The Council, which is comprised of experienced managers and employees, operates under the direction of the Deputy

Center Director for Science and is responsible for overseeing science-based decision-making across CDRH, including premarket review; periodically auditing decisions and assessing program performance; and acting as a resource for staff on scientific questions to support greater consistency in decision-making and the treatment of cross-cutting issues. We are also creating a network of experts to help CDRH resolve complex scientific issues. This network will be especially helpful as FDA confronts new technologies. In addition, we are instituting a mandatory Reviewer Certification Program for new reviewers.

○